```
131571-21-6
     EL: FEF (Fictionides)
        there in, expression in year it, preprior number incular analog with
        reduced assem, in s in irm
    ANOWER 10 OF 10 HOAFLOS CATYRIGHT 2000 ACS
     1441:55%T3 HCAFLUS
i_{n}
     114:55573
     Tonization behavior of native animatest inscalar: qK perturbation of
     Bl3-Glu in aggregates species
AU
     Kaarsholm, Niels C.; Havelund, Svend; Hongmann, Enilig
\mathbb{C}^{-1}
     Novo Res. Inst., Bajsvaerd, [K-1880, 1eh.
     Arch. Biochem. Biophys. (1990), 2%3(2), 4(4-5-1
1300
     CODEN: ABBIA4; ISSN: (0001-9hel
     de arrai
    Hinlish
    Thescale titrm. from pH 2.5 to 11.2 is used to probe solvent accessibility
     of conizing groups in Zn-free prepasa of malive and matant
     insuling. Staichlometry and p.Ka values of lumining groups in the titrm.
     curves are detd. by iterative curve fitting. Under denaturing conditions,
     the titrm, curve of human inculin is in good agreement with that predicted
     from the sum of imperturbed titrue. or the constituent identing groups and
     yierds an apparent isolonic point of b.s. Ther nondenaturing conditions
     where aggregation and puth. comur, titrms, show that only 5 of \theta
     carboxylate residues of human insulin ionize in the expected region.
     Consequently, 1 carboxylate ionization is masked and the apparent isoloni;
     point is located at pH 6.4. Correlation between ionization behavior and
     patterns of aggregation and soly. Is established by titrns, of mutant insulins and of dil. native insulin. Titrn. If an unusually sol. species,
     B25-Phe .fwdarw. His, shows that pptn. is not responsible for the masked
     Carboxylate ionication of native insulin. Titrns. of mutants Bla-Glu .twdarw. Gln and B9-Ser .fwdarw. Asy show that the masked idnication
     probably originates from monomer-monomer interactions in the insulin
     oimer. Thus, the B13-Glu side chain is responsible for the masked carboxylate ionization in aggregates turns of human insulin.
     11061-68-0, Human insulin 72751-52-1 116094-26-9
     128548-64-1
     BL: FROC (Promos)
        (ionization of, mol. structure in relation to)
1.52
    ANSWER 11 OF 17 HOAPING COPYFIRM 2002 ACC
     laraning orbit. HCAFLUS
    110:186795
    Human insulin analogs and injectable solutions containing these analogs
     and zinc ions with troiping t antillidetic action
117
    Markussen, Jan; Norris, Wiener, Laboriter, Laborite
     L v Indistri A.J. Len.
- 1
     For. Lat. Appl., Impl.
     o iku: kikuik
     Latent
     hi. 4. 1891
FAULTUT 4
                                           APPLICATION NO. DATE
     PATERT NO. FINE DATE
     _____
                             FI 214516
```

```
1441,711
     AU 612324
(M. 97124989
                                  Tage 1311
                                                                          \frac{1}{2}\frac{1}{2} - \frac{1}{2} + \frac{1}{2} = \frac{1}{2} - \frac{1}{2} + \frac{1}{2} + \frac{1}{2} = \frac{1}{2}
                            . .
                                                                          1.8000.0
                                                     nA 1 += 7 = $2 + 1
BV 1 += 7 = $ + 4 +
      ZA KONDASE
                                  1 4-5 14.2
                            Ž.
                                                                          1497000, ---
                                  19-20-25
      HU 48271
                            AL
      HU 203371
                            13
                                  19910729
                                19491129
1990080
                                                     DE 1467-315161
                                                                          130470723 ---
                           Δ.
      DD 273839
                                                                          19970722 ---
                                                     110 1957-75383
      US 4946928
                           A
                                                     11 14-7-83243
                                                                           44000
                                  19980114
                                                                          14#7012. . --
16#7012. . --
      IL 83243
                           7.1
                                 19940115
                                                        19-7-506401
      AT 49664
                            ED 1907-396401
                                                                          19470727 K--
      Ef 2061504
                            11.3
                                  19941216
                                                     JF 1967-180169
                                                                          19870721 ---
                                  19880430
      JF 63099096
                           -\hbar 2
                                                    MS 1959-424503
                                                                         19891028 ---
                                 199104]6
      US 5008241
                           A
                           19860721 <--
FRAI DK 1986-3470
     DK 1985-1135
                           19850312 ---
      DK 1.486-1070
                           19000310 ---
      WD 1986-838472
                           19860311 .--
     DK 1987-948
                           19870225
      EF 1987-306405
                           19970770 ---
                           19870720 ---
     US 1487-05550
     MARPAT 110:156795
137
```

AB Insulin derivs, having a pos. charge compared with that or human insulin at neutral pH are used to prep. solms, having prolonged insulin action. These in tilm derivs, have the structure I  $\alpha$  and  $\alpha$  tollowed by nos. in parentheses designate popular transmiss of  $\alpha$  and  $\beta$  chains, resp.; E1-E4 = Glu, neutral amino acid; X = Thr, Arg, Lys; Y, Z = amino acid in which any side-chain NH2 may be acylated and any side-chain OH may be alkylated; m, n = C, 1; R = OH, amids or enter n a 11 Shine Strapping. S.H; W . Ladi array  $+\ldots$  Array and have agreed i more charge than human insulin at pH 7 . I.e., a Basic amine acid in human insulin is substituted in the B27 position and/or a neutral amino acid is inserted in the A4, A19, B1-, and/or Eff position. The C-terminus of the Alchaun, AshAll, may be substituted by another among any to increase the stability of the The control of the co presence in trypic and control of the Till Rear intermed ate sy HELT, leader than a with FMC till, and crystal. An intermediate so in, was preparents. 144 nM Tills (wt. v I.) styrestly if wt. vf. come recoll property tive, a so see .co. only cl., and in Market Auties. The colo. Somethic Till Wash administrative for Exercit Consideration at 14.5 mm is a finally this of the attention of the first of tareatro di decisioni, al tra di la configi to the company of the property of the transfer to 7440 66 6 7 ...

111775-86-1P 111775 80-2P 111775 88-3F 117442-95-2P 117442-96-3P 117442-98-5F

```
117443-02-4P 117443-03-5P 117443-04-6P
               117443-06-8P 117443-07-9P 117443-08-0P
               120249-13-0P 120249-15-2P 120249-16-3P
               120249-19-6P 120249-21-0P 120249-22-1P
               120249-23-2P 120249-24-3P 120249-26-5P
               120249-27-6P 120249-29-8P 120249-30-1P
               120249-32-3P 120249-33-4P 120249-35-6P
               120249-36-7P 120249-37-8P 120249-38-9P
               120249-40-3P 120249-41-4P 120249-43-6P
               120249-45-8P 120249-46-9P 120249-47-0P
               120249-49-2P 120249-50-5P 120249-51-6P
               120249-53-8P 120249-55-0P 120249-57-2P
               120249-58-3P 120249-59-4P 120249-61-8P
               120249-62-9P 120249-63-0P 120249-64-1P
               120249-66-3P 120249-68-5P 120249-69-6P
               KL: PREP (Preparation)
                         (prepn. of, as antidiahetia)
               11061-68-ODP, Human inculin, analogs
TT
               RL: PREF (Preparation)
                         (prepn. of, as antidiabetics)
               120249-72-1 120249-74-3 120249-75-4
TT
               120249-76-5 120249-77-6 120249-79-8
               120249-80-1 120249-81-2
               FL: FCT (Reactant)
                        (transpeptidation of, in prepn. of human insulin anal.g)
1.58
            ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2000 ACC
              1988:596998 HCAPLUS
\Lambda N
Lan
              109:196993
              Soluble, brolonged-acting insulin derivatives. II. Degree of
ΤT
              protraction, crystallizability and chemical stability of insulins
               substituted in positions A21, B13, B23, B27 and B30
              Markussen, J.; Diers, I.; Hougaard, P.; Langkjaer, L.; Norris,
ΑIJ
               K.; Snel, L.; Soerensen, A. R.; Soerensen, E.; Voigt, H. O.
              Novo Res. Inst., Bagsvuerd, 2880, Den.
20
               Protein Eng. (1988), 2(2), 157-66
               TYPEN: PARNEY; LANG: Lost-lips
               Tournal
LA
              English
               It was previously demonstrated that insulins to which pos. charge has been
AΒ
              added by substituting P1? Florenia addition of carrie of all for the control of t
               C-terminal carboxyl group of the B-chain by amidation, featured a
               prolonged absorption from the subcutis of rabbits and pios after injection
               in solm, at acidic pH. The phenomenon is as wibed to a low coly, o mains a with the realiness by whom these analysis reputalsize as the intertant of
              reing neutralized in the tourse. However, a diameter, of insular are
demonstrable as All againstined the basistes to organism and and
              taken part in terminal of the valent appearance of the strategy of legal to a first all a taken part in terminal of the valent appearance of a capital amount of the strategy 
               position throughout the evolution. History was retained undu-
                gly line, serine, threenine, aspartit of a histidine and arginine were
```

information in this president, which is not a varying degree. In the crystal structure of the class specification is a specific to a supplementation of the contract of the co

```
amal or with A21 gly lime shower first-order assorption kinetics in give
 with a half-life of lagrant b, integendent of the Thir term. The
day-to-day variation of the absorption of this and globes significantly lower than that of the conventional insulin suspensions, a property that might render such an insulin useful in the arrempts to improve globes.
 control in diabetics by a more predictable delivery or basal insulin.
 11061-68-0 117442-95-2 117442-97-4
 117442-99-6 117443-02-4 117443-05-7
 Ell: BIOL (Biological study
          insulin deriv. prepursor, yields of, relative to fermin biomass?
 117442-94-1P 117442-96-3P 117442-98-5P
 117443-00-2P 117443-01-3P 117443-03-5P
 117443-04-6P 117443-06-8P 117443-07-9P
 117443-08-0P 117443-09-1P 117443-10-4P
 RL: SPN (Synthetic preparation); FREP (Ireporation)
        (prepr. and biol. activity and properties of prolonged-acting)
 7440-66-6, Zinc, biological studies
 RL: BIOL (Biological study)
        (substituted insulin derive, bidl. activity and stability in relation
       :0)
ANSWER 15 OF 17 HOAFLES COPYRIGHT LAST ACT
 lwab:504939 HCAFLUS
 109:1049:9
Monomeric insulins obtained by protein engineering and their medical
 implications
 Brange, J.; Ribel, C.; Hansen, J. F.; Dodson, G.; Hansen, M. T.;
 Havelund, S.; Melberg, S. G.; Norris, F.; Norris, K.; et al.
Novo kes. Inst., Novo Alle, Bagsvaerd, DK-2880, Den.
 Nature (London) (1988), 333(6174), 679-82
 CODEN: NATUAS; ISSN: 002x-0230
Journal
English
By single amino-acid substitutions, insulins were prepd. which are
 essential monomeric at pharmaceutical concus. (0.0 mM) and which have
 largely preserved their biol. activity. These monomoric insulins are
dis rhail-refult taster atter all injection than the present rapid-aring insultant. They are there is a gas or i giving diabetic patients a more physiol. plasma insulin profile at the time of meal
 consumption.
 7440-66-6D, Zinc, complexes with instilling
 Blue FBF GERNpentian;
        (bioavailability and biol. activity and self assocn. of)
 11061-68-0 11061-68-0D, zinc complexes
 12584-58-6D, zinc complexes 55599-09-2
 111479-48-2 116094-19-0 116094-20-3
 116094-21-4 116094-23-6 116094-25-8
 116094-26-9 116094-27-0 116094-28-1
 116094-29-2
 RI: BI L. R. I HELI L'ERY
        , the first \gamma and the avalent results and \gamma . It is the first twitty of
ANIMER 14 OF 17 HONDING CLETHIGHT AND ANY
 INTELLACIONE BEARLIN
 If impley gas I make a manda in a first status of the contract of the first indicates of the status of the contract of the con
```

ΙŤ

AN DU

Т1

ΑU

CS

30

DT

LA

A2

ΙT

C.

```
were prepi. By substitution with basic aming acids at the termini of the
Bedhain and my blocking the determinal carrowyl group of the Bedhain.
isceled. pH or the insulin is thereby moved from 5.4 towards physical levels. Slightly acid soins, of derivs, in which charge has been added
in the C-terminus of the E-chain, have a prolonged action in vivo, in
particular if the carboxyl group is blocked. The prolonged-acting
hydrophilic insulins crystallize instantly when the pH is adjusted to ".
The prolonged action is as wiked to this readings to wristn, combined
with a low soly,, which may be further detreased by increased comm. of
Zn ions. Hydrognobic insulins have a prolonged action independent
of the site of substitution even if the deriv. is sel. at thysicl. of:
Some derivs, were propod, from partine insulin by tryptic transportination.
N-terminal B-chain substituted insulins were projud by alkylation of a
biosynthetic single-chain insulin precursor, followed by tryptle
transcept idution rendering the double than instilling deriv. The disd.
blood glucose lowering in the rabbits implies that heither N- nor
C-terminal B-shain substitution results in substantial deterioration of
picl. potency. An index for the degree of pactraction based on the broad
grucose data is used to hombare the insplins.
12584-58-6, Pordine insulin 98743-24-9
RL: BIGL (Biological study)
   (derivs. preph. from, as prolonged asting derived)
113190-02-6P 113190-03-7P 113190-11-7P
113190-13-9P
RL: RCT (Reactant); SPN (Synthetic preparation); FKEP (Frequaration)
   (prepn. and deprotection of)
74870-09-0P 80449-79-2P 81959-12-8P
97396-48-0P 110068-63-8P 110068-65-0P
110068-80-9P 110084-28-1P 113189-92-7P
113189-96-1P 113189-97-2P 113190-00-4P
113190-01-5P 113190-07-1P 113190-08-2P
113190-09-3P 113190-10-6P
RL: SEN (Synthetic preparation); FREP (Freparation)
   (prepm. and protraction and crystallizability of, as prolonged-acting
   insulins)
113189-88-1P 113189-89-2P 113189-95-0P
Fig FFM (Synthetic preparetion, plikm) (aleparation)
    prepr. ani transpertiret. . .
113190-14-0P 113314-96-8P 113610-16-5P
RL: SPN (Synthetic preparation); FREP (Freparation)
    (prepn. and transpeptiontics of, with the called burns.
113190-12-8P
EL: SPN (Synthetic preparation); FREE (Preparation)
   (prepn. of)
ANAMER 15 OF 1" HOWELD TELEVISION AS
In all hearth on with an unit a+\psi(a) , the constraint sectors open
Markussen, Jan
1 ... 11. 4 .. . 1 2 ... , 1 - 1...
Eur. 1st. Appl., 4 pp.
THEM: FIRMIN
I at edit
Enulish
```

TT

```
11 1144 541
                                                                                                                                                                              11 1 40 4 4 4 77 7 4 1 4 5 7 7 1 1 4 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4 5 1 1 4 4
                                                                                                         - 3
                                                                                                            1.44.
                                                                                       ř.
                    F1 - + .-- -
                    4.
                                                                                                                  1... 41:
1935 - 21
                                                                                                         1944 915
1941 715
1941 715
1941 9121
                                                                                           A1
                                                                                                                                                                              Att 1944-144 Att
                                                                                                                                                                                                                                                    199,311 . --
                    ATT 6654495
                    AT (12964
JI (13128a-
                                                                                        \rm PL
                                                                                                                                                                               11 1 14 y = 1.15 y v
                                                                                                                                                                                                                                                    19-11---
                     711 h01U14h4
                                                                                                                                                                                111 - 1 \text{ and } \epsilon = 1 \approx 1.4 \times 10^{-4}
                                                                                                                                                                                                                                                     1 +4+1 -11 ---
                                                                                           i .
                   HU 201097
                                                                                                              1927/21
                                                                                                                                                                              HII - 4- W-1:24
                                                                                                                                                                                                                                                    1 10 60 511 ---
                                                                                                               199.09.78
                                                                                           1.1
                                                                                                          19+711*1
19+41714
                    Ed 552879
                                                                                                                                                                              F\mathcal{Z} = 1 + \gamma \cdot \epsilon + 0.5 \cdot 2 \cdot \gamma \cdot 7 \cdot 6
                                                                                                                                                                                                                                                    14-6 311 ---
                                                                                         A1
                                                                                                                                                                              12 1986-1666
11 1988-251
                   02 259536
                                                                                        \mathbb{R}^{\mathbb{Z}}
                                                                                                                                                                                                                                                    1-1-63-11 ---
                                                                                                          1 490, 12... *
13.4... ****
1 43. ****
                     II TRIDE
                                                                                         A1
                                                                                                                                                                                                                                                   1 +-- --
                                                                                                                                                                              AT 1 - 1
                                                                                                                                                                                                                                                    1 ** ** ** ** ** ** **
                                                                                                                                                                                                                                                  1957, Park --
                    11.1 4.44.00
                   50 5241
                                                                                           A 13915416
                                                                                                                                                                             (CD 1949-424505 19891(Z) ---
FRAI DK 1985-1135
                                                                                         19850312 ---
                   DK 1966-1070
                                                                                         1486,0310 0 ==
                   EF 1956-301755
                                                                                          19800311 ---
                   GS 1986-838472
                                                                                         19360311 ---
                    1 K 1 986-3470
                                                                                         1956/0721 ---
                    118 148 T-948
                                                                                         14670225 ---
                    12 1967-75550
                                                                                      19-7:72 ---
SI
```

```
A(1-x) = B^{\frac{1}{4}} - A(5-x) = (7ys - A(3-5)b^{\frac{1}{4}} - A(18-19) = (5ys - Asb)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                       1
                                                                                                                                                                                                                                                           B(1-6) = Cys - B(8-12) - E^3 - B(14-18) = Cys
                                                                                                                                                                                                                                                                                  \mathbb{R} + \mathbb{Z}_{N} + \mathbb{Y}_{M} + \mathbb{E}_{Y^{M}} + \mathbb{E}_
```

The title computs. (1) A and E are insulin A- and E-chain peptide iragments, resp.; E1-E4 = Glu, neutral amino axid residue; N = 1-Thr, L-Arg, L-Lys; Y, Z = amino exists (with challe moves a prop. injectable silns, with prolonged insulin action, were prepd. These prepns. may contain Znz+, preferably at 5-200 .mt. p/mt. ArgPPS-NH2 human insuein was prepd. by transportidation of H-Arr-NHL with persince invalin in the jakken elut tryjali... 7440-66-6, Zinc, and a structured by the birth of the control of t

Induction | 1.42, 1.42 | 31 81959-12-8P | 110068-58-1P

110068-59-2P 110068-60-5P 110068-61-6P 110068-62-7P 110068-63-8P 110068-64-9P 110068-65-0P 110068-67-2P 110068-68-3P 110068-69-4P 110068-70-7P 110068-72-9P 110068-73-0P 110068-74-1P 110068-75-2P 110068-78-5P 110068-79-6P 110068-80:9P 110068-83-2P 110084-28 15

```
102:179750
    Jemisynthesis of human insulin
    Markussen, Jan
     Novo Ind., Bagsvoerd, Len.
     Methods Diabetes Res. (1984), Volume 1, Issue A, 4 3-11.
     Editor(s): Larner, Joseph; Fohl, Stephen L. Fublisher: Wiley, New York, N.
     COMEN: 5300As
DT
    Conference
Lis
     English
    Methods are described for the semisynthesis of human insulin. [
hB
     11061-68-0] from porcine insulin [12584-58-6], in which
     des(Ala30) porgine insulin [39416-73-4] (tormed by 2 different
     routes) is reacted with various threonine estern. Deprotection of the
     resulting insulin determ yields numan inoutin mole. From a threshine
     residue in the caboxyl terminal positi n of the .keta.-ghain).
I P
     12584-58-6
     RL: BIOL (Biological study)
        (numan insulin prepn. from)
     74870-09-0P 76688-23-8P 80449-79-2P
1.1
     BL: RCT (Redutant); SPN (Symthetic; regularities); PREF (Frequenties
        (prepn. and deprotestion of)
     7440-66-6DP, complexes with insulin 11061-68-0DP,
     zinc complexes 11061-68-0P 39416-73-4DP,
     zinc complexes
     RL: SPN (Synthetic preparation); FREP (Fregaration);
        (prepn. of)
     39416-73-4
     RL: RCT (Reactant)
        (reaction of, with threenine esters)
LSs
    ANSWER 17 OF 17 HOAFLUS COPYRIGHT 2000 ACM
     1983:3177 HCAPLUS
AN
DN
     98:8177
ΤI
     Stabilized insulin preparations
IN
     Brange, Jens Jorgen Veilgaard; Havelund, Svend
    Move Industri Avi, Den.
Eur. Pat. Appl., Di ep.
FA
     CODEN: EFXXDW
DT
     Patent
    English
     FATENT NO.
                  KIND DATE
                                            AFFLICATION NO. DATE
                                            F.E. 1 (4) (4 1... 200 1... 1... 1... 200 4 4 4 4
                             19m20919
    EF 60141
                      132
                            1 *** 11 -1
     El 0.141
                       15
     E1 + 141
      8: AT, 1F, 111, UF
                                            "A . 104 -
                             And the second
     K = \{ \pm 1, \pm 1, \pm 4 \}
                             1.40
                                                              1 -- 1 - - - -
    HE 593413
                             144.52.24.35
                                            FF = 1 \cdot \cdots = 1 \cdot \epsilon
                                            THE 1 + 1 - 1 (* - 1)
                                                              1944 1944 1 ==
     1 K Y23137A
                            1 +-1 -411
                      ĨΝ
                            1 4961 12
                      · ·
     DK 149633
     FK 149835
                            1965 7036 ...
    1.0
```

```
19940915
19861931
19861111
                                                11:11:19:11:14:1
                                                                   1 ....
     11111111111
                        ja.
                                                18 19 5 - 14 6
                                                                    1 401 1 1 1 4 4 ==
     CH 052631
                                                AI : 4-2-5 1. 5**
                                                                    1 1-1 1 1 ---
     AT 23287
FI 78636
                                                FI 1901-717
                                                                    1 --- 15 ---
                         ř.
                               19-----
                         \zeta^{i_\bullet}
     FI 78838
                               19491010
FRAI GB 1981-7423
                         19810:10 ---
     DK 1981-4143
                       19510918 ---
                        10-00-00-00-
     EP 1982-701207
     Stabilized zinc insulin [cod-t-tz-b] proper for use in equipment
```

for entineous invalin deliver, comprises a 'a or My balt, a preservative, and optionally, a nonlogizing eshotic pressure controlling agent and(or) a pH buffering agent which lees not form a complex with either Caller Mg I has in addn. to insulin. Thus, tryst. mcnocomponent percine insulin (7.44 a) ountg. 7.4 Zn with a total activity of 200,000 IV was dissolved in 150 mL HLO contg. HOL (0.5 mL M), to this was albed 100 mL H2G contg. glyserol and PhoH 6.4 and 0.8 g, resp., the pH was adjusted with MaoH to 7.5, and the total vol. increased to 400 mL with H20. To 100 mL of this soln, was added 29.4 mg CaCl2 and the soln, starilliselby filtration and transferred aseptically to 10 mL vials. The boln, contq. 505 10 insulin/mL in 2 .times. 16-3M soln. CaCl2 had a stability factor 409.

11061-68-0D, zinc complexes ΙΤ

RL: FIOL (Biological study)

(semisynthetic, stable compns. contq. calcium or magnesium salts and)

12584-58-6D, zinc complexes  $\Gamma$ 

RL: BIOL (Biological study)

(stable compn. centq. calcium or magnesium ralts)

=2 a ib9 bib abs hitrm tot

159 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2000 ACC

1994:646581 HCAPLUS AN

DN 121:246581

- ТΙ Structural Asymmetry and Half-Side Resptivity in the T to R Allosteric Transition of the Insulin Hexamer
- Brzovic, Peter S., Chri, W.Liv F., Ermaur, Ian, Kaashing, Hiels C., Funn, Michael F.
- lepartment or brochemistry, University of California, Riverside, TA, 92521-C129, USA
- Biochemistry (1994), 33(44), 13057-20  $f: FY \mapsto FY \cap FX$ ,  $f: Y \cap Y \cap Y$

Journal LA

English

The zinc-insulin hexamer, the sterage form of involin

in the pandrous, is an all starlege twin quality in macra instance transitions between three airting conformations of star, assignated Ta, lake, and kee, on the marie of their librarial maintage portless, and otherwise Howard and the control of the contro alighteen by Lagrand (AMS). This matter that is a companies by orall changes in the positions of A-duain reciprocal and other B-duain reciprocal In this paper, the - and tw - imenal half toward EVY TH DME are used to characterize the argument in robert Total transitions of wild-type and EBL), matarit imman **zinc**-im dili **hexamers** at a toom of a color of color of the calculate to the first terms.

```
distribution of \mathbf{hexamer} contermations in favor of the k-state
 with the order of effectiveness, C.W. - W. - undert. 1- undert. Me. Anal.
 or one- and two-dimensional spectra indicate that with will-type insulin, 22N- and N3- give T3R3 species, whereas the EBlo, nutant gives an R_0
 species. An allosteric model for the insulin T to E transition based on the structural asymmetry model [F. Neydoux, et al. (1974)] is proposed
  that explains the neg. and pos. allosteric properties of the system, including the role of TERS and the action of nometry is and between picture.
 eficettors.
 72751-52-1, 13F-31n-human inscille
 RL: FRF (Properties)
         (insulin hexamer structural asymmetry and half-site
        reactivity in allesteric transition
ANDWER 2 OF 16 HOAPLYD CONTRIBUT AND ACC
  1 * *4:4011Y5 H'AFLUS
  121:1185
 A new structural type of zinc insulin observed in a magant of
 [Azi, Ser]-human insulin
 Wang, Da-cheng; Zeng, Zhong-hao; Hu, Yeng-lin; Markussen, Jen
 Inst. Blophys., Chin. Adad. Pril., Feiling, 1921, Leap. Rep. Thina Fept.: Biol. Chem., From Chin. Espt. Symp. (1993). Meeting
 Dire 1992, 241-4. Editor(s): Ed., Yu-Jang; Tam, James F.; Zhang,
  You-shang, Publisher: ESCOM, Leisen, Noth.
 CODEN: 59YOAI
 Conference
 Enalish
 The hexameric zinc insulin structure chsd. in the
 [A21,Ser]-human insulin crystal represents a new type of T3K3 insulin
 conformational state (T3Rt3), in which the conformational pattern of the
 subunits are basically T3R3, except for a numbelical stretch of P1-B3, but
 the coordination mode of zinc ions in the metal
 chelate sites adopts a T6-like type, namely 2 zinc ions
 are all on the 3-fold axis and both possess 6 ligands arranged as an
 obtahedral array. In the Fr ^3 structure, 6 wordination sites of zinc ion(II) are all occupied by the residues of insulin
 mol. itag.f, induling A Ashabo and a Higabal , which has not yet much
 which in other hexameric installs of returns. The regularity interactions between Asn-P3 and Zn(II) should be a significant
  factor for stabilizing the helical conformation of B4-B9 segment.
 seems likely that the TRR's etrusture copyelents continued, take out the translation, which may provide
  a new model for the investigation of the allosteric transition of insulin.
 A neutral org. mol., 1,4-dioxane, present in Trystn. media is most probably the effector of his conformation, which binds to a peaker on the
 hexamer surface and induses the conformation transaction the lane
 try in them at miles.
 134091-11-5D, hexamers, by Jewer with zinc
 El: IEE | Expertise
          r ni imbit n i
NAMES A SELVE ESTELLE CONTRELEGIO
 124: WORL BOARDY
 120:40:51
 Srystallegraphic Evidence : r Paul Schritzen Archet Zinc ::
 the Toke Human Instilling Hexamer
 The property of the control of the c
```

74.7

IN TI

/1.

CO

DI

LA

AΒ

.ANS.. The structure has been refined to a residual of .1% desire that independent data points to lie-.ANS. res in. The asymmetal or insists if a The dimer, and the insulin hexamer is generated by the action of the prystallog. Seferid axis. The confirmation of the insulin trimer is nearly identical to that of the Tu hexamer, while the other trimer approximates that of the Ru hexamer, except for the three N-terminal B-chain residues that adopt an extended rather than an .alpha.-helical conformation. Each of the two zinc ions , which lie on the crystallig. 3-fold axis and exhibit fwo different, disordered obordination geometries, is a criticated by the imidazole groups of three symmetry-related B10 histidine residues. The coordination sphero of the zinc in the T5 trimes is either tetrahedral, with the fourth site filled by a chloride ion, or cotahedral, completed by three water mols. The operdination of the **zinc** in the life. ANG. narrow channel in the kentrimer is tetrane-bal, with either a second chloride ion or a water m. 1. completing the coordination sphere. The putative off-axial zinc binding sites that result from the T.fwdarw.R transition of monomer II i has contain zinc ion, but instead are filled with clusters of ordered water mols. The observation that the T-state trimer contains zinc in both terrahedral and octahedral geometries has important implications for the interpretation of spectroscopic results.

11061-68-0D, Human insulin, zinc complexes,

## hexamers

RL: PRP (Properties)

(crystal structure of, for TBRS conformation with dual coordination)

ΙT 7440-66-6D, Zinc, complexes

RL: BIOL (Biological study)

(with human insulin hexamer TaRs, crystal structure of)

ANSWER 4 OF 26 HOAPLES COPPERIORS, JULY ACC 1,59

AN1994:722 HCAPLUS

120:722 DN

Distinction of structural reorganization and ligand binding in the T ΤI .tautm. R transition of insulin on the basis of allosteric models Jacoby, Edgar; Krueger, Peter; Karatas, Yasar; Wollmer, Amci

2

Inst. Biochem., Phoinisch-Westfaell, de lean. Hoensen., Aachen, Germany Biol. Chem. Hoppe-Soyler (1993), old St., eller TIEM: ECHUEI; IJJN: 0177-sbgs

ΞT Journal

LA English

ΑĐ

In all tellings a are presented in the Totalia. A transition of insulin hexamers in the presence of pheholic ligands which are based on existing exptl. information. The transition mainly involves residues 1-8 of the P-chain, i.e. 15 of the mel., which are extended in the T-candidation the heat at . The main tests to be act into it is are; the transition is smaller not time every the transition of the second trimer is annaivanteemi the relit the first her the substitute is a triber there it randition in a toperature growing classes with a larger of parts of the solution of the soluti intestination kestida, the light of and particulated in a porter made of retween two acid cent sciences, and in the lifetime of the two other dinding directly a trimer, only light when talmers can under no transits no. The two makes tall wells a DT spectros equicitins. It zinc and could incolor with the course manufaction of the appreciated in teaching to the other of the state o

of, in presente of metresol and phenol ANDWER 5 OF LO HOMELUT OF FYRIGHT L. ACT 1.1 AN 1993:1675 W HYAPL'S . 11-:200e se Chemical stability of inculin. 4. Machanismo and kinetics of themical transformations in pharmaceutical termulation Brande, Jens Novo kės. Inst., bajovaerd, EK-2000, len. .... Acta Pharm. Nord. (1992), 4(4), 214-22 CODEN: APNOEE; ISSN: 1100-1801 Journal DT LA English Insulin decomps, by a multitude of them, reactions. It seems lates at two AB different residues by entirely aliferent me manisms. In acid, deamination at AgnAll is intranclecularly catalyzed by the protomated P-terminal, whereas above pH 6 an intermediate imide firmation at residue AshE3 leads: to isoAsp and Asp derivs. The imide formation require, a carp retation. around the .alpha.-carpon/pertide carponyi carbon bond at h3, corresponding to a 10 .ANG. movement of the Bechain Neterminal. The main determinant for the rate of PS desmidation, as well as for the ratio between the two products formed, is the royal conformational structure, which is highly influenced by various exciplents and the phys. state of the insulin. As amazing thermolysin-like, autoproteolytic cleavage of the A-chain takes place in rhombohodral insulin crystals, mediated by a conserted catalytis action by several, inter-hexameric functional groups and Zn2+. Intermol., sovalent crosslinking of insulin mols. occurs via several mechanisms. The most prominent type of mechanism is aminolysis by the N-terminals, leading to isopertide linkages with the .alpha.-chain side-chain amides of residues G!nA15, AsnA18 and AdnA11. The same type of reaction also leads to revalent desslinking of the N-terminal in protamine with insulin. Disulfide exchange reactions, initiated by lysis of the A7-B7 disulfide bridge, lead mainly to formation of covalent oligo- and polymers. Activation energy (Ea) for the neutral deamidation and the aminolysis resutions was found to be so and 119 KJ/mol, resp. 11061-68-0, Foman insulin 11070-73-8, Bevine insulin ſΤ 12584-58-6, Fermine insulin 62602-61-3 EL: PKI (Froperties) (degran, of, in formulations, kinetics and mechanism :: \ MINIMAR RESERVED AND SERVED AND 1992:645709 HCAFLUD 117:245709 Altering the arsociation properties of insulin by amin and requirement Brows, favia M.; Alter, Delik A.; Persage, M. wie. J.; Chamb, E hald E.; IlMarchi, Bichard L., Green, L. Benney, I no, Harlan B., Becar, Allen H., Philelia, Tamer F., Brank, Bris H. File firstly and the transless of the second trans-Fr telm Eng. 1992 , 100 , 100 - 10 TOTAL PRESENT TOTAL CONTRACTOR Totarial Et. 1115E The importance of ir Ege and Lawide on the relifiant on. I importing was

The importance of ir has and layed with the relifiant in. I inciding was extraplinated by systematically truncation the fitter indication to the homein. The relationship is tween structure as a first subject of the relationship is tween structure as a first subject. The fitter is the fitter of t

Zn-induse is notific hexamer is ination. The is reation of numeric insuling through amin, and inequal-sments was a companied by our rotational changes that may be the same for decreased arctim. It is demonstrated that self-account a insuling on be arastically aftered by substitution of one for two sey uning agains. 11061-68-0, Human insulin 116094-23-6 133107-40-1 133107-45-6 133107-52-5 133107-64-9 144637-14-9 144637-15-0 kL: IEF (Frequeties) (redr gassers, et, C-terminal amint and in role in) 150 ANSWER 7 OF LO HUARLUD CONTRIBET 2,00 ACD 1991:4:55ac HCAPLUS 115:55580 they within if the phenylal male but give main during impulle-receptor and instain-install interactions Mirmira, Baghavehara G.; Tader, Howard J. Dep. Biochem. Mol. Biol., Univ. Chirage, Chirage, 12, corr, UNA Piochemistry (1991), 30 (33), 4222-8 CODEN: PICHAW; IDMN: DOLE-2966 James English iv using the comisynthesis of both full-length inculin analogs and their des-pentapeptide-(B26-B30)-.alpha.-darboxamide counterparts, the importance of the electronic character and bulk of the position B25 side chain both in directing insulin interaction with its receptor on isolate; canine hepatocytes and in detg. the ability of insulin to self-ass s. in sein, was examd. Analogs in the those in which inchil was replaced by eyelchexyl-Ala; Tyr; p-nitri-, p-:lucro-, p-iddo-, or p-amino-lhe; or plansing-kie in which the area, aming function has been only ated by the abetyl, hexanoyl, devanoyl, or leademantancyl memp. Findings identity that (a) the .beta.-arom. wide chain at position 822 is indeed crit. for high-affinity ligand-receptor interactions, %, neither electron withdrawal from nor electron donation to the .beta.-arom. ring perturbs ligand-receptor interactions in major ways,  $\{e_i\}$  considerable lattitude is allowed the placement of linear or rolycyclic applantmass at the year profities in permits the balles distituted and the with respect that the respect to the parameters the first attinity and to solve the commodated during the appearance appears appears as position BAS is readily accommodated during the self-assocn, of insulin monomers, as assessed by anal, tyrasing radiologination and spectrosuply scale to scale to be even although the insulin-reseptor interactions at the coll membrane in which the position 825 side chain defines the eage of intermal, contact. 103370-34-9 135393-09-8 135393-10-1 135393-11-2 135393-12-3 135393-13-4 135393-14-5 135393-15-6 135393-16-7 135393-17-8 135393-18-9 135393-19-0 135393-20-3 135393-21-4 135393-22-5 135393-23-6 135393-24-7 135393-25-8 135393-26-9 135393-27-0

RI: PIR (E) I suital processor ; TEFO In parties ; El I ocial canta, estaty; ; IFO TELEVISIA resept rainains I, to 1. Stratus in Housing t

LN

CD

 $T^{\dagger}T$ 

7.13

17

```
[ ]
          Cantelen te
         English
LA
            Next-hexarequire -80\% e^{-\gamma^2} insulin-bl4-lietal-phenylethylamide (1\% was
AA
           synthesined, and this descriptly becapentage; tide insulin was fully as
           active as infant insulin in block sluctse-segmenting and mouse on whisien
           tests. Although the formation of high-molewood aggregates of human insulin
           were dependent on Unle, the appreciation of I was Unlet independent. Thus, the complete bost and its becomings of invaling were not required for its fiel. Activity, but they were important in the formation of stable
           hexamers with Ends and is the peneration of invaling plymers.
           123583-55-1P
           RL: SPN (Synthetic preparation); FREE (Preparation)
                  (preph. and bidl. activities and preporties. wi)
T C, Ca
          AMOWER FOR THE HEARING COPYRIGHT LAW AND
           1991:136174 ROAFLOO
DR
          114:136174
11
          Insulin association in neutral solutions striped by limit station in
           Hyidt, Joeren
           Der. Chem., Risch Mati. Lai., Poskilde, IK-4 CO, Den.
           Biophys. Chem. (1991), 5*(a), 201-1:
           (WODEN: FIGHAZ; 1900: ) - 1-40.1
           ·.urr..
. . . . .
           English
ìА
          Mol. wts. and wt. distributions of sulfated, Zn-free, and SCn insulins have been measured at pH T.3 as a function of vecon. from 0.1 to 2 mg/mL by use of a combination of light scattering, retractometry, and
ΑB
           size-exclusion chromatog. Results show that sulfated insulin is manageric
           over the studied conon, range. Wt. av. mol. wts. between those of a
           monomer and a hexamer were found for both zinc-free
           and 27m insulins. Zinc stabilizes the hexamer, and
           the dimer-hexamer equil. const. is approx. 400 times higher in
           the presence of Zn than in its absence. An av. Lydrodynamic
           radius of 5.6 nm, close to the crystalleg, size of the insulin hexamer, was detd. From dynamic light scattering of 20% insulin
           sclns.
           24800-07-5D, hexamers, zinc demplement
           bL: FRE (Properties)
                   (m. . dosom. of, in neutral solns.)
L54
        ANSWER 10 OF 20 HOAFLUS COFYRIGHT 1 45 ACC
           119:130167
           The self-association of zinc-free human insulin and insulin
           analog El3-ulumamine
...
           Hammer, Jersen F.
           Brighys. Mem. Lan., Mirc Ber. Drift., Benitters, DK- et , Den.
           F. Prys. Sham. 1991 , 1991 , 1991
            tihul situak, ilika (
           1 .....
           The serit-serior. It Zn-ties hubban limiting, Zn-ties
           installing and by Fire statement, . -Zn installing and of yill anomals \ensuremath{\mathcal{C}}
           insulin in the millim lar out.m. rank was investigated by measuring the smooth pressure at pH 1.5 in ... M Natl, ... A dress. The pH apends to
           that the was reached in the gibrarie entry to the cold, and the gibrarie entry to the cold, and the
```

```
72751-52-1
         kl: FRF (Fr.; erties)
                seli-assumi ki, jä dejenden el i,
159
        AMSWER 11 OF 20 HOAFLUG COLYRIGHT 200. ACM
AN
        1989:625415 HCAFLED
111:225415
        directural transition in the megtal-tree hexamer of protein-engineered (blo Gin) insulin
         W Himer, Axel; Kannetela, Barkara; Chahl, Therpen; Meiberg, Steen J.
         Inst. Biochem., Rheinisch-Westfael. Tech. Hernoch., Aachen, Fed. Rep. Fer.
. . . .
         Biol. Chem. Hoppe-Seyler (1989), Biolist, 1941-16
         CODEN: BCHSEI; ISSN: 0177-4443
\operatorname{LT}
          Journal
         English
         for hexamer formation of native insuling the repulsive patential
         of 6 B13 Glu carbomylate groups coming together in the center is overcome by Zn binding to B10 His. Debetitution of Gla for 312 in
         position Blb by sire-directed mutagenesis, i.e. reglacement of the
         repelling carboxylates by amide groups, which are offering H-bonding
         potential, enhances assocn, and allows a metal-ired hexamer to
         iorm. Marely upon audn. of Zn ions this
         hexamer undergoes the In .:wdarw. TPRS resp. TC .fwdarw. No
         structural transition which in the native 12n insurin hexamer is
         inducible only by additives like inorg. amions of phenolic compils. [Fl:
         Sin]Insulin hexamers are transformed by themslic compds., but
         not by anions, even in the absence of any metal. The structural
         transformation of insulin can thus be brought about in 2 ways. By incrg.
         ions with the Zn ions as their points of
         attack, which preexist in the non-transformed hexamer, and by
         phenol, for which the binding sites close to the Pb histidines come into
         existence only with the transformation. Therefore transformed and
         nontransformed hexamers, i.e. mols. with helical and extended B
         chain N-terminus, must be related in a dynamic equil. Thenol acts as a
         wedge jamming the structure in the transform d state and trapping the
         Zn ions. Combination of transformed ZZn[Bls Gln]insulin
         and meral-free native invalls in the absence at adultives results in a redistribution of the Zn ions in the r -planting
         insails which is an outcome of the dynamic equil. and also demonstrates as
         influence of B13 charge on metal binding affinity. Transformation of a single subunit in a hexamer would be in the hair not at the content.
         mois, in 1 of the 2 layers terming the hexamer.
         7440-66-6, Zinc, biological studies
IT
         EL: BIOL (Biological study)
               einsuiln and insuin alle autra the structuration by the sale and h
               and a here in the recent is not
         72751-52-1
         Fir Historia of the strate that the hexamer
         ANDWER IN A FOLK HOWELPEN OF EVEN SHELLE A M
         1 44 4: 54 (714)
                                HOWELD
          111:397710
         The minimum as an arminest of the Total Forms spaticing, transits in the
          hexamer :
         e typing a fally terms to the file of a proper of the company of t
```

```
the schalt ions results in inamatic grantes in the visible
         region of the electronic spectrum and thus represents a user or
         expectroscopic method for straying the Total Altanoitien. Changes in the
           .
Sir spentral envēlope show that the agua ligang assord. With earn
         tetrahedral Cost center can be replaced by NUM-, CM-, CMM-, NM- and NCM-.
         19F-NMR empts, show that the binding of m-fritherporesol stabilizes the
        Re state of zinc insulin. The chem. shift and line breademin: In the FF singlet, which cours insulud binding, provide a useful probest the Testo Re transition. Fire to the appearance of new resonances in the
         arom, region, the 500 MHz 1H MMR spectrum of the phenodeinduced Ro
         hexamer is readily distinguishable from that or the Tolton. IH
         NMR studies show that phenoi induces the Te to be transition, butn in the
         (GlnB13)6(Zn2+)2 hexamer and in the metal-free GlnB13 species.
         Thus, metal binding is not a prerequisite for termation of the K state in
         inls matant.
         7440-66-6D, Zinc, insulin hexamer complexes
         EL: PRP (Properties)
               (Conformational transitions in, spectroscopy - 1;
         72751-52-1D, hexamers, cobalt and zinc
         complexes
         RL: PRP (Properties)
               (editormational transitions of, metal singing role in)
        ANSWER 13 OF 26 HOAFLUS CONTRIGHT 2000 ACC
         1989:400892 HCAPLUS
         111:892
        Studies on the crystal structure of Al- L-tryptophan) insulin at 2.1 .ANG.
        resolution
        Wan, Zhuli; Liang, Dongcai
         Inst. Biophys., Acad. Sim., Reijing, Feop. Rep. China
        Sci. Sin., Ser. B (Engl. Ed.) (1988), 51 12), 14.6-38
        CODEN: SSBSEF; ISSN: 0253-5823
        Journal
        English
         In order to study the pipl, effect of alterations to the N-terminus of the
         insalin A-chain, the crystal structure of Al-Cl-Trp: inculin was dott.
        was shown to belong to the trigonal system with glass none R2. The
        parameters of the unit self were a - h - mo.s .Abb., d - s... .ANG.. The
        model was adjusted and refined by using a stereochem.-restrained least
        squares program, assisted by manual revision of the model based on the
        efficiency \tilde{F} tales map, to \tilde{A} time. For the sum of the main and the enains of both Al-(L-Trp) residues in the asym. Unit were well ordered.
         It was found that the Al-Trp residue of mol. I occupied two distinct
        positions. From the results of the three-dimensional structure it was
        proposed that the 1-zinc insulin hexameric term is a
        In reductive of inciding in in a contagration of low activity. The structural action is a monthly of the
         estati militare Historia e te
         84134-94-1
                arvara. Attacture (§.
15 * ANDWER 14 OF DECEMBELOS OFFREIGHT 2011 AUG
         1489:200949 HOAFLUN
         11 .... ... ...
         Try and the first of a state of the state o
```

ΙT

IΤ

L59

AN

DN

ΑU

CS 30

DT

LA

AN

```
enformational transfermations of profine invalin, pr insulin, and
ministrainsulin hexamers ministrainsulin as a proinsulin analys
wherein the 7-dain is replaced by a dipeptibe or solink retween Gly-Aland Ala-B30). A nomenclature system is grapused in which the U-Zn
and 4-Zn crystal forms of the hexamer are designated
as the To and Take conformations, resp. For all Sproteins, 4 Mm. of S W-
reduces the rate of sequestering and removal of zinc ion
by chelator. The effect of CON- on the rate of this process sats, at the
name concn. (so mM) known to indused the To-te-To-Ed transformation in the
impulin crystal. Ther both To and ToRS conditions, order stolenionetry
for high-affinity interaction between ZnZ+ and each of the open teins is
shown to be 2 mol of Zhze/mil of protein hexamer. Consequently,
the finding that off-axial swordination of Unle via His-blo and His-Bo
residues is of minor importance for the SCh--individ Aunthoration manufactures
in a ln. is a mirmed. There To a militions, the kinetics of the reactions between insulin, promodiln, and miniproinculin and a variable excess of
terpy are similar and biphasis. The fast phase of each reaction is latorder in terpy and lst order in protoin-bound CnC+ (z=0.5-1.4). times.
184 M-1 s-1) and involves the formation of a terry-Endi- protein complex
at each zinc sites. The slow phase of each reaction is 1st
order in terpy at low comens, and tends toward a limiting, satd, value at
high terpy concas. In each system, this ster involves the rate-limiting
dissoon. At terpy-bound and, from the protein, collowed by the rapid
scoordination of a And terpy mol. and formation of (terpy)2Zn2+. Under
T3R3 conditions, the corresponding reactions for the 3 proteins are also
very similar and biphasis. When compared to To conditions, the
second-order rate const. of the fast phase is slightly reduced (): =
0.5-0.6 .times. 104 M-1 s-1). The rate of the slow phase is remarkably
reduced (k = 0.05 \text{ s-1}) and becomes zero order in terpy. The striking
similarity between the kinetic parameters shows that the same process is
rate-limiting for the reaction of terpy with the CW--induced form of cach
protein. The kinetic results indicate a mechanism where one of the two
zinc environments per hexamer is transformed by SCM-.
Thus, the slow rate obsd. under TBR3 conditions likely is limited by the
rate of the SCN--induced conformational sharps. Studies of the rate of removal of Zn2+ from the insulin {\bf hexamer} under conditions
similar to those which give any Securysta. Them provide further evidence consistent with these evidences in . Figure {\bf r}
7440-66-6D, Zinc, insulin hexamer complexes
11062-03-6D, Proinsulin (pig), zinc complexes,
hexamers 12584-58-6D, Porning insulin, zinc
 mg less., hexamers 119970-48-8
kL: PkF (Froperties)
   (conformation of, zinc-binding domains in relation 16)
ANNWER OF RECLEMENTAL TREEDRICE AND
1 ***: 1. T. 15 HOMELTS
 install temperature is a significant energy, where constrains a spin start of
malithmist, bery Hansen, Minn Heiner; Charlen, Hente Hos
Mariana, entité, les parents
Frank. Apl., .* pp.
NJEN: FIXXIZ
\Gamma_{i,i} \vdash \{\gamma_i\}_i^*
English
```

```
LOTELS B1 LOTERLS

FROM AT, PE, "H, LE, PF, PP, LT, L1, LT, NL, CE

110 8 116 The Lote Classes
         El LCTL.£
                                                                                                                        130977414 ---
                                                                                                                         1 44 7 44 14 ---
                                                        1 -4-1 -- 15
                                                                                      AT 1947-4-2450
         AT 60014
         En 2007607
CK 8706425
                                                                                      ES 1457-1124
                                                                                                                        1647.415 ---
                                                        1.4490701
                                             At.
                                                        19471268
                                                                                                                        19-71.0- --
                                                                                      1K 1367-6425
                                             Z.
                                                        1 4910 315
          PK 160460
                                           В
                                                       · 441/4410
         PK 160460
                                                       19911 31
                                                                                                                        1111114 ---
          tti r 75,33874
                                                                                     1 + < `` 1 2. 1 (, . · --
          F1 e7055-24
                                                                                     FIT TWENTERS
                                           Á
                                                        1 +871..16
                                                      19921015
          FI 87529
                                           14
          EI 87529
                                                      19930125
         No. 87(15299
                                                       19971217
                                            I_2
                                                                                     1995 기대왕 '무원건대가
                                                                                                                        1:1:00:15 ---
ERAI DK 1996-1792
                                            1867.0414
         EF 1 + 7 - 4 1/2 45
         W(1-\frac{1}{2})(4+\frac{1}{2}-\frac{1}{2})(\frac{1}{2})>0
                                           19970414 . --
         The title formulation contains .gtoreq.1 insulins or insurin derivs.,
         which in solm, in the physical pH range are presummantly present as
         monomers, to provide a fast absorption of the insulin administered.
          Des-pentapeptide (B26-3) percine insulin-B25-amide (75 mm) was dissolved
         in 3 mL aq. HCl, then 5 mL of 0.02M NaHZPO4 in 1 | phenol was added, NaOH
          to pH 8.5, and water to 10 ml. This 10 ml soln, was sixed with 10 ml z
          No glycomeckycholate in JudbM NaCl, HCl was added to pH 7.5, tilled into a
         pottle which was sealed with a manual atomizer delivering a sp. vol. per
         puff, and 100 .mu.L (10 I'm of insulin activity) was hasarly administered
          through a single purf.. A suppository centy, trisuccinyl human inculin, a
         masal formulation contg. sulfated porcine insulin, and a masal powder
          Sonty. des-pentapeptide (E16-30) porcine insulin-E29-amide were also
          formulated. Monomeric des-pentapeptide (B2v-30) porcine insulin-BCE-amide
         was absorbed faster and more reproducibly than hexameric
         Zn-insulin (human) by intranasal administration in rats.
         115038-90-9
         RL: PROC (Process)
                (nonparenteral formulation of)
          39416-70-1
          Rb: RCT (Reactant)
         'pertide durling :, With ply graphenylarany.phenyre anyrems de' 12584-58-6DP, Insuling is, ..... 97123-35-8P
          RD: SEN (Synthetic preparation); FREE (Fregulation)
                (prepn. and masal formulation 01)
          11061-68-ODP, trisuscinylated
          Ali Ebbl Iregalati n
                (prepn. of, for masal administration)
          11061-68-0, Insulin (human)
17
          P.L.: FROC (Prodess)
                 sa minulari no t
          lektik en Babia
Literan
          Notice that the property of the second proper
          strer divalent sations
          inttrop, Pomar I.
         of Androne English Med. Red., Adet. Natio. Third., Staderra, cold, Adetralia
Blok. Shem. Hoppe-Peyser 1986, and by , as ter
```

```
hexamers and hexameric appropries; in these white laber,
          I was present as species up to an including tetramers. In a lns. cents. This and Daze, moremers and impers it appeared to be the only species present. The significance of these findings, esp. In relation to a ryle for Dake in the action of inculin, is discussed.
          7440-66-6, biological studies
ŢΫ
          RL: BIOL (Biological study)
                  (insulin despent groption analys soli-are, the industion syl
          55599-09-2
          FL: PRP (Properties)
                 (self-assecon. c1, divalent rations effect in)
1.5.9.
         ANSWER 17 OF AC HUAFLUD CULYRIGHT ... C AND
          1986:1926BE HOAFING
AN
1: 4: 1 . 1 . . 1
          Growth of single prychald of MeAlathapita Instillingual their merray
          crystallographic analysis
200
          Min, Liwen; Charg, Minha; Wan, Indi; Lians, Captal
CG
          Inst. Riephys., Anad. Sin., Belding, Fest. Rep. Thina
:::)
          Kexue Tongbao (Foreign Lang. Ed.) (1985), 30(8), 1109-11
          CODEN: KHIFBU; ISSN: 0454-0949
           Turrhal
1.A
         English
          Single crystais of (b-Alajbo pig (nsu.in (1) [100469-14-5] were
isto.
         prepd. and hwamd. by x-ray prystallog. Tryptals were grown in a kuffer
          contq. citrate and, except for pH, optimal conditions for crystal prowth.
          were similar for those for pig insulin 2-Zn rhombohedral
          crystals. Isomorphism of I with A-Zn pig insulin was very good
          with a difference of only t. . in CH-axis. Results indicated that neither
          the mode of close packing of the hexamers of I in unit cells nor
          the essential conformation of the mol. was greatly enanged. However, the intensities of reflections were changed and the diffraction data for i
          differed considerably from that of 2-{\bf Zn} pig insulin. Thus, partial conformation of the I mol. was changed somewhat compared with 2-
          Zn pig insulin.
TT
          100469-14-5
          FI: IFE [Projection.
                   review in the second of
L59 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2000 ACS
          page: succed Educities
An application of the rotation function method to the determination of the
          crystal structure of (L-Met) PS-insalin-orbin: ation of the molecules in tre-
          unit coll and atrial etrumbral model
          Par, Cile, 1st, 1st); thens, thereis
          Inst. Bighys., Asai. Cln., Belting, Feg. Beg. Chin.
          Then will Holawige Following to William Richard 1985 ( 1985)
           1 DENI: INDEED: DENI: - - - - - -
7.14
          The calculation in \pi 1 in the physical attraction in
            I-Metaba-instalin 199102-79-15 taking the structure of
          rhombohedrai v-Zn an a model was varried at. The non-
          htyptallin. .-to a smir, which was related to the company of a direct, was hexamer as an other to the company of the company of hexamer as an other transfer of the company of the company
```

```
BL: BET (Frantant)
        reaction 2:, with zinc, principlin in relation to
 - fil 1e4
FILE 'REGISTRY' ENTERED AT 11:25: 2 ON 27 DEC 25 OF USE OF THE TERMS OF YOUR STUDY OF A GREEKENT. FLEASE SEE "HELD COASETERMS" FOR DESTAILS.
COPYRIGHT (1, 2004 American Chemical II to by "A W.
CTRUCTURE FILE VIDATES: Lo DEC 2005 HIGHEST EN 311-12-23-3
TO WE IMPORTATION NOW CURRENT THROUGH PROVER, INC.
 Hillease note that search-merm priming when apply when
 socialisting SmartSELECT course. S.
Structure search limits have been increased. See HELL SLIMIT
for details.
* + d 121 sqide dan tot
L21 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2000 ACS
   253597-48-7 REGISTRY
   2: PN: US6011007 SECTO: I an laimed protein [44] (TA INDEX NAME)
    PROTEIN SEQUENCE
SQL 30
type ----- location ----- description
ur.gommon A--a-1 - -
ungammon Aaa-3
ungammun Aaa-1
     1 XVXQHLCGSH LVEALYLVGG ERGFFYTFKX
SEQ
    Unspecified
    CA
     JTN Files: GA, CAPLUS, TOXLIT, USFATFULL
              I REFERENCES IN FILE CA /1947 TO LATE:
              I FERTHERN FOR IN BINE MARIN. LA I DATE
APPEARINE OF INCIDENT
```

COE, TO: I also also approve in the Company Market NAME.

ILL ANGRE OF FEBRUARY OFFE FOR

253597-47-6 HE HATTEY

1:-EU: UCF-11 1 1 EROTEIN CHAPTEIN

21

RN

Fis

: T-

```
1 BEFERENMENTIN FILE MARILLAND TO LATE:
1 REFERENMENTIN FILE MARILLAND 1 MINOR LATE
```

REFERENCE 1: 174:33-64-

me i sqide cam tot lide

```
ANSWER 1 OF 1: RESISTEY - WEYEL HET 2 % A W
     207519-94-6 REGIATRY
[\cdot,\cdot]
\{(1A+z)A, ((1B+z)B)\} + InStable (notion), zolik-[N+-]N+((1a)) plane, index a con-
     hyoroxy=k4-oxocholan=k4-yi]=k-,alpha,-j.utamyl}=k-lelysin=k- (901) k-, k-
     HYGIGAY 24 .
INDEX NAME)
```

 $\mathbb{R}^{n}$ FROTEIN DEGGENCE

SQL 50,29,21

t ype	] w	cation	her ription
irrije Eradje Bridge			divultide Eridge dipultide Eridge dipultide Bridge
GEQ 1	FVNQHLOGOH LUKA	IMMUT ( EBOFFYT)	E K
	GIVEOCCTSI CÉLY 421 NGV 080 Se	OLENYO U	
	: FEFERENCE	S IN FILE CA ( C TO NON-SEE)	
SEEE EFTTE	1: 1::::::::		
REFERENCE	2: 132:31:702		
1.			

FFFFFERTTE : Indianage L REFERENCE 4: 15:54,947 L 1/11/11 12/17/12 of in the silver sale \* HIRPTI and the second of the second o

ANSWER LOFT SERVICIAN OF FERILED LOST AND

BEBERTH ": T. HIT H

207519-93-5 FERRICTER

Institut Shoman , Institut Shoman S

51,30,21

```
-: FILHIAM DUBALYLU BESPETTET
                   -1 GIVE, COURT COLFULENTS N
SEG
MF
          C251 H4L1 Ne5 Obl Se
CI
          MAN
\mathbb{C}\mathbb{R}
           r^{\alpha} \bar{p}_{1}
                                 MA, MAILMO, TOMBLIT, MUFATEMIL
I REFERENCED IN FILE MA 140 TO LATE
I PEFERENCED TO IMM-PLECIFIC DERIVATIVED IN FILE AM
                                 1 REFERENCES IN FILE CAPIUS (1967 to DATE)
REFERENCE 1: 113:1138
LARCH ANGWER & OF 12 PRSICERY CALVELUE ACC
BN 207519-92-4 REGISTRY
        FROTEIN SEQUENCE
1:11
S.J. 51,30,21
NTE multiphair.
        - modified (modifications unerpecified)
 ______
 type ----- location ----- description
_______
bridge Cys-7 - Cys-7' absultise bridge bridge Cys-19 - Cys-20' disulfide bridge bridge Cys-6' - Cys-11' disulfide bridge
SEQ 1 FUNCTIONS INVESTIGATION OF ERSEPTIFIEST
          1 GIVEQCCTSI CSLYQLENYC N
SEQ
MF
          C281 H421 N65 080 S6
CI
           MAN
SR
           THE PLACE OF A, MARKET, TORILL, SCHAFFULL OF REPRESENTED TO PLACE ON THE STATE OF A STAT
                                 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)
REFERENCE 1: 12:11:12
1,1
          ANSWER 4 OF SECREGISTRY CONTRIGHT AND ACC
RN
        207519-90-2 REGISTRY
          51,30,21
          (r-\epsilon,1), \epsilon (\epsilon - m-\epsilon,1) , at , the charge value \epsilon
type ----- i wati n ----- kanija n
tridge type — type" dibultige fright
fridge type" with a type ! First parties
fridge type" type ! First parties
```

```
DEFERENCES IN FILE CARLING TO DATE

1 BEFFERINGS TO INMOSE SIND DEFINATIONS IN FILE CAR
1 BEFERENCES IN FILE CARLING LIMIT IN DATE
 REFERENCE 1: 127:19an
LCD AMSWER 5 OF 55 REGISTRY CONTRIGHT 1840 ACT
                    207519-89-9 REGISTRY
                    Insulin (numer), LPB-(NG-[4-]7-[Gl-pare xypent decyl vanife, ethoxy]-1,4-aicxcoutylj-L-lysine(- G(X)) (GX INTEX NAME)
                    PROTEIN SEQUENCE
 E:3
 JOL 51,30,21
 NTE multichain
                   modified (modifications unspecified)
   type ----- iscation ----- isocription
  bridge Cys-7 - Cys-7! distillie bridge bridge Cys-19 - Cys-20! distillie bridge bridge Cys-6! - Cys-11! distillide bridge
 UEQ I FUNCHLOGER LYEALYLVOG ERGFFYTEKT
 SEQ 1 GIVEOCCTSI CSLYQLENYC N
 MF
                   C279 H432 Not 082 96
 CI
                    MAN
 물론
                   CA
                    STN Files: CA, CAPLUS, TOXLIT, USPATFULL

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 LC
                                                                 1 REFERENCES IN FILE CAPLUS (1963 TO DATE)
 REFERENCE 1: 129:1028
 1.69 ANSWER 6 OF 53 REGISTRY COPYRIGHT 2000 ACS
                    207519-88-8 FFOICTHY
Institute the time of time of time of the time of tim
 DN
                PROTEIN SEQUENCE
 FS
SQL 51,30,21
  modified (modifications unepecified)
  type - --- location ----- Hermintian
Triap type" - type" at line rails rails by the type to the type type to the ty
UP, I FUN, HUSSUB INFACTIONS PERFECTERI
                     1 HIVE COUNT ON PRINT NO
NEW HALF DEED ON THE
                    2000
```

AMBERS S

```
Insulin (numan), LAR-[Ne-[4-], l- mark@mytride tyl.aminu]-1,4-dl.m @utyl]-l-lydine]- HOL: /OA INDEM MAME:
    PROTEIN OF TENCE
S.A. 51,30,21
NTE multiphain
    medified 'medifications unspecified'
_____
type ----- Rotation -----
                                         amentip tium
bridge Cys-T - Tys-T' alsalfide tribue bridge Cys-19 - Cys-20' alsalfide bridge bridge Cys-6' - Cys-11' diralfide bridge
_____
       - 1 FWMOHLOSCH LABALYLAGG ER-FFYTIKT
SEO
        -1 GIVEQCOTOI CSLYPLENY) N
    0275 H414 N66 OP1 Se
MF
22.1
    MAN.
SR
    40A
    OTH Files: CA, CAPLUS, TOWLLT, USBATFULL
I PREFERNCES IN FILE CA (1000 TA) LATE
              1 REFERENCES TO NON-SHEDIFIC SERVIATIVES IN FILE CA
              1 REFERENCES IN FILE CAPLUS (1967 TO DATE)
REFERENCE 1: 129:1028
160 ANSWER 8 OF 53 REGISTRY COPYRIGHT 2000 ACS
RN 207519-85-5 REGISTRY
CN Insulin (human), 29B-[N6-(4-Benroyl-L-phenyl llamyl)-L-lysine)- ((3/1) (A-Benroyl-L-phenyl llamyl)-L-lysine)-
INDEX NAME)
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
    modified (modifications on genified)
type ----- i satto ----- accomption
______
bridge Cys-7 - Cys-7' disultide bridge bridge Cys-19 - Cys-20' disulfide bridge bridge cys-h' - Cys-11' disulfide bridge
    SEQ 1 FVNQHLCGSH LVEALYLYCG ERGFFYTPKT
    THE PLANT AND MELTIN, I RELEASED TO LATE IN THE WHITE INTERPRETATE A THE TOTAL ATE.
PERBERNIE II II. HILLE
   ANIMPER OF THE PROTECTION OF THE PROTECTION OF THE
     207519-84-4
```

```
ieriaae
ieriaae
                                                           iria:e-
                   I GIVEÇOTNI DELYÇLENY'I N
OLDU HA W DET COW DO
MAD
                               1 FVWQHLCGCH LYEALYLYCG EFGFFYTIK
  MF
                     C.A.
  ŝĸ.
                     STO FILES: CA, CARLUE, TOWLLT, CURATFULL

REFERENCED IN FILE CA (1.0 TO LATE)

REFERENCED TO NON-SERVIFIC REPURTIVES IN FILE CA

REFERENCED IN FILE CARLUE CASE.
  REFERENCE 1: 124:1418
  LUG ANSWER 10 OF 55 REGISTRY COPYRIGHT 2 Jan ACC
  RN 207519-83-3 REGISTRY
  FS PROTEIN JEQUENCE
  S./L 51,30,21
  NTE multichain
                modified (modifications unspecified)
  ______
   type ----- location ----- description
  bridge Cys-7 - Cys-7' disalride bridge bridge Cys-19 - Cys-C' disalride bridge bridge Cys-6' - Sys-11' disalride bridge
  SEO 1 FVNOHLOGSH LVEALYLVOG ERGYFYTEKT
 i mivegocial cultylento n
                    TOTAL HART DATE OF THE
  ME
                     MM
  0.1
 ŚĒ
                     DTW Files: CA, CAFLES, TOXILL, COLUMN
                                                                A MARRIED IN FILE WAS INCIDENT OF A SECURITY OF A SECURITY
                                                               4 REFERENCES IN FILE CAPLUS (1967 TO PATE)
 REFERENCE I: I: :: 1 %: - 1 % !
  PERFECTE : In this to
 PERCENTURE 1: 1. C. I. F.
  ICO ANOMER II FOR BESILTED OFFICED AND
                      207519-82-2 HE TOTET
  1.11
                       In rulling in the rule of the results of the rule of
```

```
nilaje dys-u' - @yr-ll' ilrililie irlaje
      i Funghiradh lubalylu ib ekaffyuldu
   1 GIVEQUOTO1 2014, LEHYA N
Clos E400 NGC OYA AC
MF
1
   MAN
: !.
    7- -
    CIN Filer: M, WHING, T MUIT, WHATFULL
             1 REFERENCES IN FILE (A ,1967 TO EATE)
             1 REFERENCES TO NOW-SHESHES SERVATIVES IN FILE VA
             1 PEFERENCES IN FILE CALLY (1907 I CATE)
REFERENCE 1: 129:172-
LOU ANSWER IN OF 53 REGISTRY POPERSHET TO MANY
EN 207519-80-0 REGISTRY
(2) Insulin (framan), MAR-(Net(theory)) the wytheletwop (appropriate) yether (extry to (Westernament)).
    INDEK NAME)
FG PROTEIN SEQUENCE
SQL 51,30,21
NIE multichain
   modified (modifications unspecialled)
______
              ----- location ----- denutitien
_____
bridge Cys-7 - Cys-2' disultile bridge bridge Cys-6' - Cys-11' disultile bridge bridge
SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTFKT
     1 GIVEQUOTRI CSLYÇLENYO N
    $266 H397 N65 O78 S6
ME
    MAN
    175
\mathbb{S}\mathbb{R}
    JTN Elles: CA, CAPLUS, TOXLIT, USPATFULL

1 REFERENCES IN FILE CA (1967 TO PATE)

1 REFERENCES TO NON-CERCIFIC TERMINATURE IN THE PARENCES TO REFERENCES TO RELEASE.
KEFERENCE 1: 129:1028
Les ANIMER SHIP FOR HEILUTEY TOWASHED . As
   207519-79-7 FE HATEY
1. 1.
    insalis beman , letterible , teal. Feletys .yuteleTyclocie te ti
    III EN HALF
    FROED TRANSPORTE
   51,30,21
NTE maitidimin
    madiji i proditration saspedities
Type ---- initial ---- printer.
```

```
111
              STE FILE: "A, CARLUE, TERLIE, WHATFULL

I REFERENCES IN FILE A 1 %" TO TALE

I REFERENCES IN FILE WASHING TO TALE

I REFERENCES IN FILE WASHING TO LATE!
 PEFERENCE 1: 129:1/28
 100 ARDWER IN OF 50 RESISTEY CONTRIBET OF ACCOUNT
          207519-78-6 REGISTRY
              insurin (numan), 298-[Me-coy (chemyl costy))-L-lysine]- (*11) . W INDEX
            NAME)
 F_{ij}
             IBUTEIN SEQUENCE
 51,30,21
 NTE maltimain
            modified (modifications unspecified)
  type ---- invation ----- icanition
DEQ 1 FUNTHLOOCH LYEALYLVON ENGREYTIKT
SEQ 1 GIVEQCOTOI COLVQLENY I
          0265 H-95 M65 875 36
MF
17.1
             MAN!
            (A)
 SR
             STN Files: A, CAPLES, TOKLIT, CREATFULL
1 REFERENCES IN FILE CA (1947 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 LC
                                         1 REFERENCES IN FILE CAPLUS (1967 TO DATE)
REFERENCE 1: 129:1028
 Den Annwer in Bonk Beninder Nachlief Gerin
             186003-66-7 REGISTRY
 hill
             Insulin (human), 298-(Nd-(1-exchemationv1)-L-lysine)- 1901 CA IN EX
             ir Himlir, mit
 UQL 51,30,21
 NTE multichain
            modilie: [medifications on persite:
 otga. Hereer volstå blerere i skultbugtvik.
IN THE REPORT OF THE PROPERTY OF THE PROPERTY
```

```
REFERENCE 1: 1::1:41**
 3: 132:29395L
 REFERENCE
                                                131:100-12
 REFERENCE
                                      4:
 REFERENCE
                                      A: 150:94 % le
 REFERENCE
                                      6: 130:542905
                                       7: 190:325405
 REFERENCE
 4: 12.7:1~~11
 REFERENCE
 REFERENCE 10: 129:1028
  160 ANGWER 16 OF ST REGICTER CHIRACHT A VEAC
 RM 175895-36-0 REGISTRY
                insulin (human), zeb-[No-,1-exetetrade yr -1-lysine]- reft (CA IMPEX
               NAME)
           PROTEIN SEQUENCE
 FS
 SQL 51,30,21
 NTE multichain
            n.:dified (mcairications unspecified);
                                                     ----- iocation ----- despription
bridge Cys-7 - Cys-7' disultide bridge bridge Cys-19 - Cyr-21' disultide bridge bridge Cys-6' - Cyr-11' disultide bridge
 _____
neo i fragerosse i vedleza m se servicen
                   i givkomatal palyolenya n
                270588-46-0
 DR
               0271 H409 Ne5 67A CA
174
                STE Files: CA, CAPLUE, TOWLIT, USEATFULL

1' REFERENCES IN THE TA TIME TO INTERFEL A FILE VALUE OF FEFFER AND THE FILE VALUE OF TAKEN AND THE FILE VALUE OF TAKEN AND 
 LC
                                     * *: *
                                      : . . : . . :
FFFFFFFFFF
                                      -: 1:::: :. +=+f.
4: 1:1:1:0 +:1...
```

```
REFERENCE 13: 129:135-
           ANOMER IN FIRE REMOTER OFFICER. AND
           169535-38-0 REGISTRY
           1-9-legitide (synthetic e-amin, avid extension, turion protein with
           .alpha.-factor receptor (Caronarymy ex relevisiae leader pertide) fooi n
           protein with pertide (synthetic 5-amint asil turil protein with Insulin
Bechain (1-arginine, (1-arginine) thumant of the 1700 INDEX NAME
OTHER NAMES:
           19: PM: "Souliob" (Epil: 4% daimed gratein
111
           PROTEIN SEQUENCE
FS
SQL 146
                    1 MRFESIFTAV LEAGUSALAA HUMUTTEDET AQIDAKAVIO YODLESIFEV
SEU
                  - I AMLIFONOTN DOLLFINITI ASTRAKEROT OMAKEREARA KARREMU, HI
                101 COCHLYBALY IN CORRESPRY TEMPROTURE, WITCH CLY, LEMYON
MF
           Unspecified
CI
           MAN
JR
           No. 7
           STN Files: CA, CAPLUL, TOMLIT, USFATFULL
                                  2 REFERENCES IN FILE CA (1967 TO LATE)
                                  1 REFERENCES IN FILE CAPLUS (1967 TO DATE)
REFERENCE
                           1: 132:73643
REFERENCE 8: 123:322102
160 ANSWER IN OF SECRETARY CLEVELOST L. F ADD
           169535-36-8 REGISTRY
F.N
           1-6-Feptide (synthetia: fasian protein with .aip.a.-14 to receptor
            (Santharomytes derevisiae leader peptide, tastch protein with peptide (synthetic 5-amino abid) tusion protein with insulin 5-shain (1-argining)
            (human) (901) (CA INTEX NAME)
OTHER NAMES:
           21: PN: US6011007 CEQID: 48 dimed protein
           PROTEIN SEQUENCE
FC
q_{i} \neq v \mathsf{T}
         145
                    1 MREFCIFTAV LFAAGSALAA EVETTTEDET AGIFAEAVIG YODLEGDEDV
aEQ
                  51 AVLPESNSTN NGLLEINTTI ACIAAKEEGV SMAKREEAEA EAREVUQHLO
                101 COHLVEALY: MONEPORETT INTENTIFIC OUTSIDELY, I RULET
\sim 1
          MAN
SR
          CA
          STN Files: CA, CAFLUS, TOMLET, CAFATFULL
LC
                                      PEPEPENGEN IN FILE WELL IN TO LAIR
REPERKUTA VI LOGI HAR
Des Angwer 19 Fift Felloter Streight L & L.V.
          169535-34-6 REGISTET
           Being the product of a first of the contract of the contract of the contract of the product of the contract of
          All the control of th
```

```
Charle ditied
              MAL
                1.64
                                            : MA, MARINO, TRMIT, MCRATEMLI
I REFERENCES IN FILE MA (1.4 T. :ATE)
I REFERENCES IN FILE MARINO (1.46 TO LATE)
               DIN Files:
                                   1: 1:0:3:4-
REFERENCE
REFERENCE
                                  a: 1. v: 52 21.02
160 ANSWER 20 OF 53 REGISTRY COEYRIGHT 1969 ACC
            169535-32-4 REGISTRY
EUN
               Receptor, .alpha.-ractor (Saccharomydes verevisiae ceaser pertide) : mi n
              protein with protine (synthetic Seaming a very facion protein with Insulin is-chain (slearginine) (buman) (FII) (CA INTEX NAME)
 ON 15: FM: CCCC11000 SEDIC: 39 Claimen : rate in
F33
              FROTEIN SEQUENCE
1901 137
                          I MREPSIETAV LEAASSALAA PUNTTTEDET WOLFERNIS YSBLEDDEDU
                        51 AVLIFSKSTN MULLFLEGTI AGURAKERGU SMAKRFURJH DOGSHLVEAL
                    101 YLVCGERGEF YTHKTEGIVE COCTOLUCLY CLENY W
MF
              Unspecified
CI
               MAN
SR
              CA
               STN Flies: CA, CAPLUS, TOWLET, "SPATFULL
                                             2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAFLUS (1967 TO DATE)
                                    1: 132:73648
PEFERENCE
REFERENCE
                                   2: 123:322102
LGG ANSWER 21 OF DE REGISTRY COPYRIGHT 2000 ACC
              169535-30-2 PEMISTRY
RM
Peptide (Sarchardmy ear veretical mynthetic) mailed logace in on protein with peptide (synthetic S-amino acid) fusion protein with insulin
               (human A-chain) fusion protein with insulin (human plus P-Main) (921)
              (CA INDEX NAME)
   11
                H: PM: US6711087 SE,ID: 36 claimed protein
E. E.
             PROTEIN SEQUENCE
351. 102
                       TO EXPOSE TO THE WAY FOR THE CONTROLS FOR CASE TO A CARREST AND A CARREST FOR THE CARREST FOR THE CONTROL OF THE CARREST FOR T
              THE RESPECTATION OF MILE, CONTRACTION OF ACTIONS OF ACT
```

```
JTHER NAMEN:
  ZN – 11: EN: MOV. 11500 VE, II: ex el dize i protein.
                     IN TELL BE TELLE
                140
                                      1 MKFESIFTAV LEARCYALIA EUNTTURDET A, 11 ABAUL E NUTLE METU
                            61 AVLĒFODOTM MOLLFINOTI APIAARRE V SILRFFUN,R LISARLURĀL
121 VLUMBRISFF YTIKOLIARS IVE, DIDIZ SUY, LEDYDI
                     The position i
                    Mani
                    ....
1.1
                    STN Files: CA, CAFLER, TOMELT, WHATFULL 2 REFERENCES IN FILE CA (1907 TO PATE)
 LC
                                                             D REFERENCES IN FILE CALLUS (1907 T. LATE
REFERENCE
                                                 1: 1:2:7:645
REFERENCE 2: 123:322102
LOU ANSWER 23 OF 53 REGISTRY COPYRIGHT 2000 AND
               169535-26-6 REGISTRY
EM
1.11
                . Frotesin (Saccharomytes resevisiae y{	t EAT} ) general Claimy {	t x}_0 of {	t x}_0 -popular.
                     inclin protein with paptine (synthetic 5-amino acid, rusion protein with
                     Insulin A-chain (61-glyving) (numan, fusion protein with insulin B-chain
                     [3-threonine] (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
                   9: PN: US6011007 SEQID: 30 daimed protein
CN
                   FROTEIN SHOUENCE
FS
COL 104
                                1 MKAVFLVLOL IGFTWA, FUT GLESSVETFE ESLITAENTS LANVAMAKKE
51 VTQHLOGSHL VEALYLVUGE KGFFYTEKSS DAKGIVE, GC TOSCOLY, LE
                            101 NYCG
MF
                    Unspecified
CI
                   MAN
\mathbb{N}\mathbb{R}
                   PA
                   oth Filse: MA, MAILUO, T MIIT, MEALFULL
C EFFERENCE IN BILF MAIL OF I LANE!
                                                              2 REFERENCES IN FILE CARLOG (1967 TO DATE)
REFERENCE 1: 132:73648
FEFERENCE 2: 103:320102
164 ANNER 24 OF 53 RESIDTED TOTAL HELD AND
FN 169535-24-4 FF HATEY
                 . Бастында сүүлүн байман баймын жарымын жарымын байын 
                   a landson good to the Within Champion of Liberty Tone Common store in America.
Within Champion of the grant of a common to the common store of the
    AR TEIN DE, TENTE
                                                                                         indigned in the state of processing
                   104
                               I MRAUFIUUS ESE WALEUT STELDETEE ESTIDAEUT DAUWAAFEE
1. ST.HI SASEL VEASELUS ESE SESSEN SOR SON DE SESSEN DE
```

```
REFERENCE .: 12 1: 111 ..
             ANNWER OF THE BEHINDRY OF FROM INC. AND
 1.1
              169535-22-2 RESIDTET
             Peptide (Garmaremyres receviriae synthegib si mal LaTtilliques filmin
             protein with pertide counthering each for it institutes with institution. Aschain (zie arenine) shumang rusi noprotein with Institute he shall institute nine) shumang rusi noprotein with Institute he shall
 OTHER NAMED:
            Ti PH: TV: 11 1 JW, H: 14 tidmes; r tein
               FROTEIN CEQUENCE
 Ē.J.
SQL 104
                          1 MKAVFLVLSL IGF WAQIVT GLESUVEIFE EMILIARRIT LAUVAMAKKE
                      51 MIQHIC WHL VEALYLYS SE FOFFYTHESE MARRIMEGOS TOTOSIN, LE
                   HOL NYCK
MF
              Unspecified
CI
              MALL
1111
              \Omega A
              STR Files: CA, CARLUS, T MLIT, UNRATFULL
L REFERENCES IN FILE (W. 1962 TO LATF)
IN REFERENCES IN FILE (WILLS) 1967 TO DATE
1 / 1
                                  1: 1:2:7:045
REFERENCE
REFERENCE
                             2: 113:323102
160 ANSWER 26 OF 53 REGIDTRY CONVENENT 2006 A W
             169535-20-0 REGISTRY
Peptide (Sascharomyces derevisiae synthetic sidnal LaCl Espa3) funith
             protein with pertide (synthetic of ne pAKIve i-amine with fusion protein with insulin A-chain [21-alanine] (human) tusion protein with insulin B-chain [3-aspartic acid] (human) (9CI) (WA INDEX NAME)
OTHER NAMES:
            S: PM: USCOllog PEGID: 31 oldingd recoll
             PROTEIN SEQUENCE
1.163
             104
                           I MKAVELVISL IGECWAGEVT GDERSVEIPE ESTITAENTT LANVAMAKRE
بالعالم
                       51 VDQHLCGSHL VEALYLVCGE RCFFYTFKSD DAKGIVEÇGO CSICSLYÇLE
                   101 NYCA
               1... :- .:.. 1
(']
              MAN
SE
              CA
                                          CA, MARLMA, INBLIL, MURATEMIL
REFERENCES IN RILE WOLLD LAIF
LEREFFERMENT IN RILE WESTER LAIR LAIR
              CTN File::
PRINCE LE LE FALTE
              ANYWER OF SPIRE PERSONER OF FRESHED LOUGHWAY
1
1-11
              169535-18-6 REFLUERT
              Factor Calphan, prepries Caronar myres services of deep FFDIs. sens MFL administration of the control of the co
```

```
FO FRITZIN CALCENTE
140
                            1 MRFEGIFTAV LEARODALAR EVNTTTEDET AJIPARAVIG FULLEGUFUV
S1 AVLEFSNOTN NGLLFINTTI ADIAAKEEGU GLOKBEVNJH LUGDHUVBAL
101 YLVOGERGFF YTEKODDAKG IVEJUVTSIO GLYJLENYGU
-111
                    Unspecified
 NE.
111
                   MED
. :
                   THE PERSON IN TARLET, TOWARD, TOWARD THE CONTROL TO FATE)

PREPERENCES IN FILE (WELLOS 1967 T) DATE:
                                             1: 1:2:176.49
 REFERENCE
REFERENCE 2: 17: 12:172
 160 ANGWER 28 OF 53 REGISTRY CHARACTER DESIGNATION
F.15
                   169535-16-4 REGISTRY
: 11
                  Teptide (Salpharomyono cerevidiae clone pAKloo synthotic signal
                   LaC212spx3) fusion protein with 1-29-instlin (human of ne pAKis- Be main fusion protein with popule (synthetic 5-amina acid studion protein with
                     in sulin (number clone paking A-chain) (601) (62 INFEM MAME)
OTHER NAMES:
                3: PN: US6011007 SEQID: 15 / Laime i protein.
CN
                  Teptide (Carcharômyres derevisiae clone pAKIS: symthetir signal
                   LaC212spx3) rusion protein with proinsulin deletion derivative (30-serine,
                    Fl-ascartic acid, fl-aspartic acid, bb-alamine, pd-lysimed (moment clone
                    pAK188 isoform MIS)
                   PROTEIN SEQUENCE
 판단
SOL 104
                                  1 MKAVELVLSL IGECMAQENT GDECGNEIFE EGLIIAEHTT LANVAMAKRE
                                51 VNOHLOGSEL VEALTLYCGE RGFFYTIKSD DAKGIVEQCC TSICCLYQLE
                           101 NYCM
                    Unspecified
(11
                   MAN
                   CIL FILM: CA, CAPLUS, TOMBET, USPATFOIL
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPITO (1967 TO LATE)
REFERRIME 1: 152:75648
REFERENCE 2: 323:322102
                   ANAMER . * For PERSONER OF EVELOPIES AND
                   169148-75-8 BE WATER
                    TiA-, tA , the december in the morning, the time of a compact system and a compact system.
                  The supplied of the second of 
   THEF TA INDEX MAMENT:
              on the provided from the control of the control of
```

```
bridge Type-P' - Type-P' Heartle-Gridge
                            1 REMEMBARTY NIHL COMMUNICAL FALVIOUS GRANTER
                                 1 TRGIVEDOOT GIAMBY, LED YOU
SEQ
                 #1534 Hille New Oa7 Se
MF
CI
                 ĽΈ
                   1
                  TTN Files: CA, TAILNO, TEXLLI, TURATFULL
                                                     E REFERENCES IN FILE (A (1967 TO DATE)
                                                      1 REFERENCES TO NON-MEMBER PERIVATIVES IN FILE (A
2 REFERENCES IN FILE MARINE (1986) TO LATE:
FEFERENCE 1: 1-2:7 0-45
REFERENCE D: 12 1: 12112
 LEO AMOWER 30 OF L. AUGISTRY COPIES HIT 3000 ACT
RN 169148-74-7 REGISTRY
                  (1A-21A), (1B-29B)-Insulin (frman), MA-(L-throungleb-argingl,-NB-(L-, agma.-
glutamyi-L-.alpha.-qlutamyi-k-alanyi-L-.alpha.-dlutamy.-L-alanyi-i-.alpha.
                  gratamyl-L-abshyl-1-arginyl,- (ETE) (FA INDEX NAME
OTHER CA INDEX NAMES:
               (1A-21A), (1B-29B) - Insulin (human), WA-(NM-L-throughlel- n sinyl) - MB-(NM-(M-
                   [N-\{N-\{N-\{N-\{N-\{N-\{N-1\}\}\}\}\}-1\},a\}] ha.-platamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamya-1-alamy
                 -glutamyi)-L-alanyi]-b-.alpha.-glutamyi!-L-alanyi}-b-arjinyi}-
 FS PROTEIN SEQUENCE
SQL 60,37,23
NTE multichain
             modified (modifications unspecified)
  type ----- location ----- description
 bridge Cys-15 - Cys-9' disulfide bridge bridge Cys-20 - Cys-20' disulfide bridge bridge cys-9' - Cys-10' disulfide bridge
SEQ 1 BEABARARY NOHLOGSHLY BALYLYCCER GEFYTEK
                     CI
                    12 to H45 : Nati 094 No.
                 MAN
SR
               CA
                THE FILMS: OA, CARLING, I KLIN, THEATHNIL

LEFFFERITE IN BUILDING THE TAIR

BEFFERITE IN THE HERITET THE TWITTE IN SOME TWO
BEFFERITED IN BUILDING THE TWITTE
F#01F10 # ... : 1 : 1
APPEARNIE ... Indicate
                  ANSWER OF SECURITIES OF FERDING
                  169148-73-6 EF HOTEY
                   the large to the large of the large to the l
```

```
1 FVNQHLCGSH LVEALYLVCG EROFFYTEKT
        1 GIVEÇOCTSI COLYÇLENYO N
SEQ
ME
    C286 H428 Net O52 Se
Cit
     MAN
Cik
    STN Files: CA, CAFLUL, TOWLIT, USEATFULL
2 REFERENCES IN FILE CA (1967 TO LATE)
3 REFERENCES IN FILE CALLUD (1967 TO LATE)
LC
PEFERENCE :: 141:7:44
REFERENCE 2: 123:322167
LOU ANSWER 32 OF 53 REGISTRY TOPYRIGHT 2000 ACC
RN 169148-72-5 REGISTRY
   Insulin (human), 298-[No-](P.alpha., S.meta.)- = hydr wy-z4-exdendian-d4-y1,-
    L-lysine;- (701) (CA INLEX NAME)
    FROTEIN SECULNCE
MQL 51,30,21
KTE multichain
   modified (modifications unspecified)
_____
type ----- location ----- description
bridge Cys-7 - Cys-7' disulfide bridge bridge Cys-19 - Cys-20' disulfide bridge bridge Cys-6' - Cys-11' disulfide bridge
SEQ 1 FUNOHLOGSH LYEALYLYCG ERGFFYTEKT
    i Prive, romani and e, desira da
Granije-ej-a
    C281 H421 N65 079 S6
Hir
CI
    MAN
$R
    CA
        Fig. 8: A, Walle, T. MLIT, WEARFILL

3 REFERENCES IN FILE WA (1967 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

2 REFERENCES IN FILE WARRING (1967 TO DATE)
PERFERING IN 1911 THE 19
INDEPENDENCE IN ENTIRE
IN ANOMER SOUR OF BEHINDER CHERRISH L. AV.
FN 169148-71-4 REGISTRY
```

```
-1 FULLHI 1988 DUERLYDUG EESFFYTEKT
            1 GIVEQUOTOI COLVÇLENYU N
Ç280 H404 14 NGC UVU DE
MF
            MAN
\cdot\cdot \bar{\Xi}
            offic places: TA, CARLIC, ITELIT, TOTALFULL

L REFERENCES IN FILE TAILUTE (1901ALE)

L REFERENCES IN FILE TAILUTE (1901 DELATE)
REFERENCE 1: 132:73(4)
REFERENCE 2: 1/7: %22102
LOO ANSWER 54 OF 55 REGISTRY COLYRIGHT 2000 ACC
RN 169148-70-3 REGISTRY
 Insulin (human), 29B-\{Ne-\{k-\{k-\{k-\{k\}\}\}earboxy-1-oxopropyi\}arkine\}eihoxyj+1-
          oxohexadecyl]-L-lysine]- (901) (TA INDEX NAME)
FS FROTEIN SEQUENCE
.ÇL 51,30,21
NTE multichain
         modified (modifications unspecified)
_____
 type ----- location ----- description
______
bridge Cys-7 - Cys-7' disulfide bridge pridge Cys-19 - Cys-20' disulfide bridge bridge Cys-6' - Cys-11' disulfide bridge
DEQ 1 FWNQHLOGSH LVEALYLVÖG EKGFFYTFKT
                   - 1 GIVEGOCTOI OULYÇLENY: N
SEC
MF
TI
            0279 H422 N66 082 96
            MAII
OA
" [I
LC
            STN Files: CA, CAFLUS, TOXLIT, USPATFULL
                                     2 REFERENCES IN FILE CA (1967 TO DATE)
2 PEFERENCES IN FILE CALLED THE FILE (ALLED THE FILE)
REFERENCE 1: 132:73648
REFERENCE 1: 123:32216.
       ANAMER OF BUILDINGS THE SET OF ANY
            169148-69-0 FF HATEY
           Therefore you man and the design of the contract of the contra
          51,30,21
        maită de ale
         m diffied om diffrations omepositioni
 _____
```

```
22.0
            eth filed: Ta, Callie, Tallie, Tolaifull
Lamberenced in File Wollfull Tate
Lamberenced in File Mailing (1967) To Late
REFERENCE 1: 171:73648
REFERENCE d: diminute
Low ANSWER SO OF IT REGISTER OWEREIGHT IN A M
          169148-68-9 REGISTRY
           1. 7
3,4. 51,30,21
NTE multichain
          modified (modifications unephrifital)
 ______
 type ----- identified ----- sourception
SEQ 1 FUNDHLOSCH LVEALYLVÖG ERGFFYTEKT
             1 GIVEQUOTOI COLYGLENYO N
: NF (*)
MF
           C276 H416 N66 081 S6
CI
           MAN
SR
           STN Files: CA, CAPLUS, TOXLIT, UPLATFULL

3 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES TO NON-SIECUFIC DERIVATIVES IN FILE CA
LC
                                    5 REFERENCES IN FILE CAPITO (1907 TO DATE)
PRITERIOR I: 102:75046
REFERÊNCE 2: 129:1028
PERFECTE : 1 %: "
LOO ANSWER 37 OF 55 REGISTRY COPYRIGHT 1907 ACC
           169148-67-8 REGISTRY
RN
         Insulin (human), 198-186-18-1 - Par My-18 majourly, arun 508-
Emergaiotyl]-1-Lyclin - Philosophia MADE
LE TEIN SE, TEIN D
51,30,21
type ----- satisfication ----
 enise tyse" - Tyse"! Hi litia esise esilen tysel: - Tyse"! Si litia esilen tysel: - Tyses ! Si liti
```

```
A REFERENCES IN FILE SALING TO LATE LATE CAPITY OF THE LATE
        1: 1:4-
REFERENCE
KEFERENCE 2: 128:512101
LEAR ANDMER - OF SECRETET CONTRIBUTED A V
AN 169148-66-7 REGISTRY
   Insulin (human), 208-(Ne-jo- 4-ny moxy-t,5-111.d phony: -/,1-111.1 -l-
   PC
   PROTEIN SEQUENCE
∴22 50,29,21
NTE multichain
   modified (modifications unspecified)
type ----- To sation ----- description
_______
bridge Cys-7 - Cys-7' distilide bridge bridge Cys-19 - Cys-20' distilide bridge bridge Cys-6' - Cys-11' distilide bridge
SEQ : FVNQHLCGSH LVEALYLVCG ERGFFYTTK
SEQ 1 GIVEQUETSI COLYQLENYO N
MF
   C272 H392 I4 N66 O&C D6
   MAN
35
   CA
   STN Files: CA, CAPLUS, TOMLIT, UDFATFULL

3 REFERENCED IN FILE QA (1967 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
LC
           3 REFERENCES IN FILE CAPLUS (1967 TO DATE)
REFERENCE 1: 132:73648
REFERENCE A: 110:100
REFERENCE 3: 123:322102
160 ANSWER 39 OF 68 REPLATED TO STREET HIT I'M AND
   169148-65-6 Harrist
  Insulin (human), 198-[N0-1]4-(4-hydroxy-3,5-diicdorhencxy)-3,4-
   diiodophenyl]acetyl]-L-lysine)- (GCI) (CA INTEX MAME)
   IROTEIN SEQUENCE
F'S
50,29,21
maltiof fr. ifflation angestates
+g... ----- : 1.1. 1. -----
```

```
REFERENCE 1: 1: 1: 1: 4:
REFERENCE Z: 123:172-
                               -3: 123:3211 %
REFERENCE
LOU ANSWER 4, OF 5% RESISTED CONTRIBUTE STATE
           169148-64-5 FEGIETRY
HII
               (!A-21A), (!P-19F)-Insulin (hyman), U9F-[No-,1-,xsnewadesys,-h-lymine]-
          (901) (CA INDEX NAME)
FROTEIN DEJUENCE
FS
SQL 50,29,21
 NTE miltichair.
             omo ditio d'Emodificatione compection de
         ______
 tyre ----- lacatila ----- secutitin
______
hridge Cys-T - Tys-T' dicultide hildge
bridge Cys-19 - Tys-ke' disultide bridge
bridge Tys-6' - Tys-11' dicultTide bridge
SEQ 1 FUNDHLOGSH LUFALTLUGG ERGFFYFFK
SEÇ
                   1 GIVEQCCTSI CCLY,LENYC N
            270598-29-8
DR
             0269 H400 N64 OTE 36
MF
CI
             MAN
SR
             CA
             STN Files: CA, VALLES, TOWLIT, USTATEVLL
11 REFERENCES IN FILE CA (1967 ID LATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
11 REFERENCES IN FILE CAFLUS (1967 TO FATE)
REFERENCE
                                  1: 133:9108
                                 PERMIT
                                3: 132:298852
REFERENCE
                                  :: ''=: ''t'
REFERENCE
                               5: 131:106812
LEBERTY'E
                               ola (j. 1805). Programa
ELEVEL DE LA SEC
                                  4: y 3:
BEFFERNY : Letters
PEFERENCE IN CONTRACT
IN AMERICA, A PART REST OF SECTION OF SECTIO
169148-63-4
```

```
type ----- lynation ----- iostription
 _____
hridge Cys-C - Cys-C' displicate bridge bridge cys-ls - Cys-L' displicate bridge bridge bridge cys-e' - Cys-il' displicate bridge
                 : FUNGHERSON INEMERICAN ENGINEER
                     1 GIVEÇÇCTDI COLYÇLENYI N
SEQ
           371305-44-4, 276595-25-5
DR
MF
          7267 H402 N64 O76 Se
( • •
          MAN
1.
           47A
              THE FIGURE - ACCUMENTER, RESID, MA, MEDUL, MARRAME, LIFT, DRUMEL, LEFT, LEFT, DRUMEL, LEFT, LEFT
           I REFERENCES TO NON-WEBSIEFF DEBINATIVES IN HILE UN.
                                  25 REFERENCES IN FILE CALLS (1907 TO CATE)
                             1: 1-3:277798
REFERENCE
                            z: 135:193472
REFERENCE
                            3: 133:115250
REFERENCE
                            4: 15:34496
REFERENCE
                            4: 133:9104
REFERENCE
                            6: 152:315772
REFERENCE
REFERENCE
                          7: 132:298852
PEFERENCE
                         9: 132:77648
PEFFER
                         1: 2:1:201:10
REFERENCE 10: 131:252834
160 ANSWER 42 OF FIRSTINGS TILES IN A ...
          169148-62-3 REGISTRI
No Insulin (human), 29h-[Né-(l-exodecyl)-L-lysine(- (901) (CA INTEX NAME)
FS PROTEIN SEQUENCE
35,4L 51,30,21
NTF meltidlik
         om diilea moditivati not mogetiiles o
 rigg.
inline "yve" - "yre" Histiin riine
priine "yve" - "yve" illiniin riine
rrida "yve" - "yve"! illiniin riine
```

```
T PERFECUENCE IN FIRE WILLIAM IN THE
```

```
REFERENCE
            1: 131:72-48
REFERENCE
            1: 1:0:342993
               130:325450
REFERENCE
            ::
```

REFERENCE 4: 129:1828

L: 125:158els REFERENCE

6: 124:127039 REFERENCE

REFERENCE 7: 123:3021/2

```
160 ANSWER 43 OF 53 REGISTRY CONTRIORS THOSE ACC
```

RN 169148-61-2 REGISTRY

CN Insulin (human), NA-[(1,1-dimethylethoxy, mark-nyl]-Nk-[]], l-

ES PROTEIN SEQUÉNCE

SQL 50,29,21 NTE multichain

modified (modifications unspecified,

\_\_\_\_\_\_ ----- location ----- description \_\_\_\_\_

bridge Cys-7 - Cys-7' disalfide bridge bridge Cys-19 - Cys-20' disalfide bridge bridge bridge bridge bridge

SEQ 1 FYNQHLCGSH LVEALYLYCG ERGFFYTPK

1 GIVEQCÒTSI ÖSLYQLENYO N N 67 H 996 D476 + 1 05 SEQ

 $\mathbb{M}_{\mathbb{R}}$ 

.....

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USEATFULL 2 REFERENCES IN FILE CA (1947 TO DATE)

l BEFERENCES IN MINISTER SERVICES (1967 TO BATE)

PEPERENCE 1: 152:2-648

ERRERUM .: L. .......

CANADA AND ELECTRIC CONTROL OF STATE OF

EN 169148-60-1 PERMITEY

SIAPLIA (Albeith Pinicon Suran (Core in Pole Tropos, Albeith Sola (Core in Pole Tropos) This can in the make The Thin ingress the

3,1 50,29,21

NTF multiminin

\_\_\_\_\_\_ . . . . . . . . . . . . . . .

```
MF
UI
             City Hand Not Oliver
             MAN
 SE.
              CK
                                        CA, CAELUG, I ELIT, TURATRUIL
4 REFERENCES IN FILE CA 1907 TO SATES
1 REFERENCES IN SILE MALUW LIGHT TWO IN FILE MA
4 REFERENCES IN FILE MALUW LIGHT TWO LATE
              SIN Files:
                              1: 152:73648
REFERENCE
                              ..: 120:102.
REFERENCE
REFERENCE S: 185:15-419
REFERENCE 4: 123:322102
 160 AMERIK 45 OF US REGISTRY SAVALSHI . C. AME
RN 169148-59-8 REGISTRY
CN Insulin (number), 268-(No-((Serylexy) arbonyl]-L-lysine)- (901) (CA INDEX
            HAME)
FS FROTEIN GEOVENCE
SQL 50,29,21
 NTE multichain
           modified (modifications unspecified
 _____
                                             ----- logation ----- description
bridge Cys-7 - Cys-7' disulfide bridge
bridge Cys-19 - Cys-20' disulfide bridge
bridge Cys-6' - Cys-11' disulfide bridge
JEÇ 1 FVN,MILGBCH LVEWLYLVCG EASFFYTEK
SEV I GIVE, ROLE THE THEFT H
CI
             MAN
SR
              . TV - F1 1. 3:
                                             CA, CARIUS, TOMBIT, UNFATFULL
                                         REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
                                         * PEFERENCES IN FILE CAPLUS (1967 TO DATE)
TERRET HOUSE THE STATE
in the first in the second sec
PRINTER OF LOCALIDA
DO ANIMER DE POSE REMOTER OFFICION AL
           169148-58-7 REFULRY
             (Marxia), TRacelle almost in the member of the Tarket see production and the
                     50,29,21
```

```
i dive more cone, yene ch
2.35 Hode to 4 Stelle
MF
CI
      MAN
SE
LC
      CL
                  : CA, CAFLUS, TOMLIT, POTATFULL

* PEFERENCES IN FILE CA (1 + 0 T ) LATE

1 BEFERENCES TO NON-SERVETO DEBIVATIVES IN FILE (A

** BEFFRENCES IN FILE CALIDS 1367 1+ LATE
      PTN Files:
REFERENCE
              1: 136:73646
FEFERENCE
               1: 129:130.5
               1.00:104763
REFERENCE
REFERENCE
              4: 125:15able
REFERENCE
              5: 184:127/69
REFERENCE
             - w: 167:920142
10 - AMOMER AT OF DECREO LITEY OF EVALUET DOWN AND
FN 169148-57-6 HENTSTEY
CN (1A-21A),(1B-29B)-Insulin (human), 39F-(10- 1-excursionyd)-L-lysine(- 1-15
      (CA INDEX NAME)
F3
     PROTEIN SEQUENCE
SQL 50,29,21
NTE multichain
     modified (modifications unspecified)
type ----- location ----- description
bridge Cys-7 - Cys-7' disultide bridge bridge cys-19 - Cys-1' distillar bridge bridge bridge bridge bridge bridge bridge
LE, I FUNDALOGER INEALYLVOR ERGFETTEK
          1 GIVEOCOTSI OSLYGLENYÖ M
     1 Green L. d. Co. 16
31
      MAN
SR
      CA
     OTN Files: CA, CALLUS, T.ELLT, C.SATFULL

4 PREFERENCE IN FILE A 1.6 I ALE

1 PERFERENCE IN FILE WELLT OF FILE A

4 PERFERENCE IN FILE WELLT OF TO THE
LC
FFFFFFF
            FFFERANTE -: 1.5:15 -- 1.
EDEFERNITY II TO I HAVE I I
```

```
hrline Cys-' - 'ys-'' distrible briane
bridge Cys-i9 - 'ys-'' distrible bridge
bridge Cys-o' - 'ys-ll' distrible bridge
SEQ
                     1 FVNOHLOGGE IMFALYLMOG ERGEFYTEKT
                       -1 Brun, Crit Thin, Limit i
             C264 B367 Ne5 578 C6
MF
CI
             MAN
ЭR
             CA
             STN Files: CA, CARLUS, TOMLIT, USPATFULL

- FFFRENCES IN FILE VA 1 0 1 LATE:

- REFERENCES TO NON-SPROIFIS BERIVATIVES IN FILE CA
LC
                                          REFERENCES IN FILE CAPLUS (1967 TO LATE)
                              1: 132:73648
REFERENCE
                              2: 129:1028
REFERENCE
HUFTERINGE
                           LGG ANSWER 49 OF 53 REGISTRY MORTRIGHT 1996 AND
RN 169148-55-4 REGISTRY
CN (1A-21A),(iB-29P)-Insulin (human), 29H-[N6-(1-oxodecyl)-L-lysine]- \PCI:
             (CA INDEX NAMÉ)
FS PROTEIN SEQUENCE
SQL 50,29,21
NTE multichain
           modified (modifications unspecified)
 type ----- location ----- description
 _____
pridge Gys- - Gys-' Hisultide bridge
bridge Gys-18 - Gys-1' Hisultide bridge
bridge Gys-1' - Gys-11' Hisultide bridge
 ______
SEO 1 FYROHLOGON LVEALYLY TO FROFFYTER
SEO
                     - 1 GIVEOCCTSI CSEYOLENYC N
ME
           -0263 Ha94 N64 O36 D6
0.1
             MAN
            THE BOARD WAS TRUENDED TO DESCRIPTION OF A PREPARED TO DESCRIPTION OF A PROPARED TO DESCRIPTION OF A POWER OF 
FREELENCE
                                ... j∂r.jrwwja
BEFERRINE
```

```
51,30,21
NTE militain
```

1784	:	~	Swaiptin.	
bridae	0ys-19	- 198-01	displications	
bridge	0ys-19	- 198-111	displicate in the	
bridae	0ys-6'	- 198-111	displication of the	

1 FVNOHLOGGH LVEALYLYCG ERGFFYTIKT SEC

SEC 1 GIVEQUOTCI ESLYPLEMYO N C165 H389 N65 CCR S6

ME MI MAN

CK 1.75

LC

STN Files: CA, CAFLUG, MAGREAGI, TOMLIT, UCHATFULL B REFERENCES IN FILE CA (1967 1997). 3 REFERENCED IN FILE CALLUD (1967 In CATE)

REFERENCE 1: 1.:0:100.5

Frenklice 2: 125:245454

REFERENCE 3: 121:222192

160 AMSWER 51 OF 53 RESIDTRY OFFICIANT COST AND

RH 120177-51-7 REGIDTRY

Insulin (rattle), NA-{(1,1-limethylethoxy, surbonyl}-xA-L-threonine-loA-L-isoleutine-29B-(N6-[(1,1-mimethylethoxy) parabnyl}-L-lyeine'-sob-co-L-alanine- (3CI) (CA INDEX WAME)

OTHER CA INDEX NAMEC:

3,4,44,45,90,91-Hemathia--,11,14,17,20,20,20,20,30,30,30,30,41,44,51,54,50,00,63,66,69,72,75,78,81,84,56-hematorastableyological filtric nonacontaine,

cyclic reptide deriv.
Insulin (ox), NA=[(1,1-dimethylethoxy) turbonyl]=8A=L=thre ninc=1 A=1=
1. Telline= (felice, li, l= imethylethoxy) turbonyl]=8A=L=thre ninc=1 A=1=
1. Telline= (felice, li, l= imethylethoxy) turbonyl]=8A=L=thre ninc=1 A=1= . . . . . . . . . -

1:11 PROTEIN SEQUENCE

SQL 50,29,21

NTE multichair

es diasto modifications unspecifica

t ype	lecation		description	
		- 1 t		
- (	1975 = 1 1 1975 = 1 1			

```
olog karang mengang mengangkan kenanggan beranggan beranggan beranggan beranggan beranggan beranggan beranggan
. .
```

. It stypy that analytems to the state of the t

117.11

```
ON (1A-21A), lib-25B - Insortin (noman (90)) W INTEX NAME
FIREA CA INDEX NAMEO:
    cyplic pertide deriv.
     Insulin (cm), wA=L-thpernine-1(A-1-incleutine-4)b-de-L-alanine-
OTHER NAMES:
    - Paralanine-Bell-insulin (por sine)
    Des(B (C clamine) pip inculing
Tes(BCC insuling ixmun
(1<u>11</u>
    Des-B30-alamine-insulin (province
    Desalamine-(P30)-pordine insulin
PROTEIN CEGMENME
Fill
   50,29,21
NTH multimals
______
type ----- location ----- description
______
riide (798-7 - 298-2) dismiride midge
bridge (798-19 - 198-20) dismiride bridge
bridge (798-0) - 290-11 dismiride bridge
_______
SEQ 1 FUNORLOSSH LVEALYLVOG ERSFFYTPK
SEQ
        -1 GIVEQCCTSI CSLYÇLENYC N
    121796-35-8, 130587-81-4, 120020-05-1, 109697-99-4, 0.722-42-7, 74870-05-6, 78642-50-9, 144687-10-1, 36159-00-9, 31959-09-7, 54566-0 -1, 282528-78-3, 289054-43-9
DR
MF
    C253 H376 N64 C75 D6
\in !
    MAN
    STN Files: CA, CAFLUS, CASREACT, MEDLINE, TÜMLIT, UNPATFULL
87 REFERENCES IN FILE CA (1967 TO LATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
87 REFERENCES IN FILE MAILUS (1967 TO LATE)
FEFERENCE 1: 133:1754 ..
            2: 133:99679
REFERENCE
           2: 71:4777
REFERENCE
           4: 131:63454
REFERENCE
REFERENCE
           6: 140:30.74.
REFFERENCE
           - #: - 1..+:151-9-
EFFERENCE 1: 100:...100.
  11061 68 1
```

```
Human insulin
CH
       Hammal Im
\mathbb{C}\mathbb{N}
       Humulin R
       Insulin (Cercepitheeus ae mices.
CH
CN
       Insulin (Macaca fascicularis)
CN
       Insulin (Macaca mulatta)
       Insulin (Fan trouledytes)
711
CH
       L-Threonine, h-pnenylalanyl-L-valy:-L- asparatinyl-L-alutaminyl-L-histiayl-
       b-leuryi-L-Systeinylgiy yi-L-seryi-L-histidyi-L-leuryi-L-vaiyi-L-laipna.-
       glutamyl-1-alanyi-1-lea yl-1-tyrosyl-1-lea yl-1-valyl-1-systeinyiglysyl-1-
.alpha.-glutamyl-1-arginyigly yl-1-phenylalanyi-1-phenylalanyi-1-tyrosyl-1-
threonyl-1-prolyl-1-lysyl-, systic (".twdarw."),(1;.jwdarw."))-
       bis(disulfide) with glycyi-L-isoleucyl-L-valyi-L-.alpha.-qlutamyl-L-glutaminyl-L-cysteinyl-L-cysteinyl-L-cysteinyl-L-seryi-L-isoleucyl-L-cysteinyl-L-seryi-L-isoleucyl-L-cysteinyl-L-seryi-L-ieucyl-L-.alpha.-glutamyl-L-asparaginyl-L-tyrosyl-L-cysteinyl-L-asparaginyl-L-tyrosyl-L-cysteinyl-L-asparaging cyclic
       (('.fwdarw.ll')=disulfide
1717
      No-volin R
ON
     Fénfil R
QN
     Ultraphane
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
______
type ----- invarion ----- impription
______
bridge Cys-7 - Cys-7! disaltide bridge bridge Cys-19 - Cys-10! disaltide bridge bridge Cys-6! - Cys-11! disaltide bridge
SEQ
      1 FVNQHLGGSH LVEALYLVCG ERGFFYTFKT
             1 GIVEQCCTSI CSLYQLENYC N
SEQ
      CNET H363 N65 OTT D6
COM, MAN
MF
         TW FILES: AGRICOLA, ARBOLINE, AMAROTE, BIOPUDINECO, BICCIO, BI TECHUI,
TA, CANTERLIT, CALLUC, CACREACT, CENE, CEN, CREMCAIS, CHEMLIST, CIN,
CSCHEM, DDFU, DIOGENES, LRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE,
       SUN Files:
          IFICDP, IFIPAT, IFIUDP, IMCDIRECTORY, IFA, MEDLINE, MRCK+, FROME,
          PTETO, TVINE, T WIST, CON, CO
             ('Fire contains numerically searchable property data)
       Other Sources: EINECS:*, WHO

(**Enter CHEMLIST File for up-to-date represent y information)

47: REFERENCE: IN FILE TAKE TO LATE

1. PEFERENCE: TO INHOUSE THE TAKE TO INFORM
                - 1: - 1: -: -: 44 - -4
               FFFFEN EN M.
REFERENCE 3: 1 N:17%T-48
PEPERENTE 4: 1991 Tests
                : : : . .
```

```
PEFFERENCE 1: 1:3:1:1:000
er diide wan liri
139 ANSWER 1 OF 1 REGISTRY COPYRIGHT COUR AU
      23713-49-7 KEGISTRY
      Zin, in Chi; (ed), di la luiem NAME
OTHER NAMES:
CN
     Zinc cation
(11)
      Zinc di ation
      Zinc divalent ion
711
      Zir.: i.e.
      Zinc i.m(2+)
      Zinc(2+)
CN
CN
      Zinc(II)
C11
      Zing(11, Cation
CN
      Zina(II) ion
CN
      Zn2+
MF
      Zn
      STH FILES: ACRECOLA, ANARCTE, FIGHERINISC, FIGURE, FICTECHNO, CA, CAPLUS, CACREACT, CEN, CIN, DIFF, LETHERMS, CRUCT, EMBASE, IFICEB, IFIPAT, IFIUDP, NIOCHTIC, HIRA, HROMT, TOMLINE, TOMLIT, USPATFULL, VETU
LC
          ('File contains numerically sear hable property actag
Z::2+
                *67% REPERENCES IN FILE CA (1967 TO DATE)
17% REPERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3090 REFERENCES IN FILE CAPLUS (1967 TO DATE)
REFERENCE
               1: 134:10149
REFERENCE
               .: 154:151
                3: 134:100:5
REFERENCE
FFFFFEN F
REFERENCE
               5: 1/3: /67479
BEFEERINGE
```

1 . 1.

FFEFFER T

FREEDEN F

BEFERENCE:

The state of the s

10: 1: 4: 4: 5

```
F. 1
       Film retail
        F 2000
ÇN
       F 20% (metal)
       18 8
LC 1 (element)
LS 4
In the tall
        NC-Zirm
Rheindink
       TF (metal)
ON
       VM 4Flo
        12799-65-2, 1991/1-69-4, 194.-1-61-4, 2 ****--4:
DR
ME
        ...r.
CI
       COM
       STM Files: AGRICOLA, AIDULINE, ANABSTR, AFILIT, AFILITA, AFILITA, AFILAT, AFILAT, FICENCIA, FICTOR, FICTOR, TA, WEA, WHITE FROM, WALL, CALLUS, CASREACT, CROP, CEN, CHEKCATO, CHEMINFORMER, CHEMINST, CHEMINES,
1
           CIN, COCHEM, CONE, PIFO, DETHERM*, DIOGENEO, DIFFR*, DRUGU, EMPACE, HODE*, IFICOB, IFIFAT, IFITDE, INCLIFECTORY, IFA, MELLINE, MRCK*, MSDS-OHD, NAPRALERT, MIGGHTIS, FILCOM*, FIRA, FROMT, RTECO*, TOWNINE, TOXLIT, TULCA, ULIDAT, USPATFULL, VETU, VTB
         ('File contains numerically searchable property data' ther Jources: | LOLL', EINED'', LOTA''
              (**Enter CHEMLIST File for up-to-date regulatory information)
Zri
                134420 REFERENCES IN FILE OR (1970 TO TATE
                 10306 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
```

```
194020 REFERENCES IN FILE WALLS IN TO LAIR, I APPRAISHED IN FILE SATURDS FOR THE LAIR.
REFERENCE
         1: 134:1.857
REFERENCE
          REFERENCE
             194:184:7
          3:
ar ng right ta
          • • •
1 4 1 1 1 4 4
*: 14:1.
```